



# SURGERY

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and Science of Surgery

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# SURGERY

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## Original Communications

### Symposium on Cancer of the Breast

#### EXPERIMENTAL INDUCTION OF MAMMARY CANCER\*

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THE mammary gland is a frequent site of neoplastic changes not only in man but also in several other species of mammals. It is one of the commoner tumors of the mouse, the dog, and the cat, but is rare in the cow.<sup>19</sup> By far the greatest volume of experimental work on mammary tumors has been performed on mice. Rats and rabbits, at least of special breeds, have been used successfully by some investigators, and more recently work on mammary tumors of dogs has been initiated.

Since most of the developments in this field have not reached the stage of clinical application, they are not generally appreciated, although they have contributed much to the understanding of the cancer problem in general, and of mammary cancer in particular. Especially fruitful have been the studies on the etiologic factors involved in mammary tumors in mice.

#### INVESTIGATIONS ON MICE

One of the earliest published descriptions of a mouse mammary tumor was made by Crisp in 1854. Scattered descriptions of a few tumors appeared in the literature between 1891 and 1906, in connection with experiments on transplantation of tumors that had their inception and development during that period. Apolant, in 1906, made a noteworthy contribution in his exhaustive and accurate description, classification, and consideration of pathogenesis, based on the study of 276 tumors. Additional studies by Borrel, Michaelis,

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\*Sections of this paper dealing with mammary tumors in mice are essentially a condensation of papers in the recent symposium on Mammary Tumors in Mice, written by members of the staff of the National Cancer Institute.<sup>2, 15, 31, 61, 62, 69</sup> References given in that volume are not reduplicated here, and reference is given only to papers that have appeared subsequent to the preparation of the book, or those dealing with species other than the mouse.

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J. A. Murray, Haaland, and others permitted the conclusion that these tumors are malignant epithelial new growths of the mouse, identical in nature with similar tumors of man.

Mammary tumors in mice originate multicentrically from the cells of the mammary epithelium. The tumors may arise from any portion of the mammary tissue, which in the mouse extends over the whole subcutaneous area from behind the ears to the base of the tail except for small midline ventral and dorsal strips. The subcutaneous tumors, readily detected by palpation, grow progressively, and spontaneous regression is rare although by no means unknown.

Microscopically, numerous morphologic variations between different tumors and different areas of the same tumor are encountered. Although in the majority an adenomatous pattern revealing its relation to or derivation from glandular structure is evident, arrangement may be in compact masses, and papillary, cystic, and hemorrhagic areas also are frequent. More rarely, keratinizing, and mollusoid forms may be seen, and a few tumors contain neoplastic connective tissue elements as well, forming carcinosarcomas. Despite these variations, however, the tumors form a pathologic entity, and for most purposes the term "mammary tumor" is adequate. Cytologic investigations of the tumors demonstrate no fundamental changes in the nuclei of the neoplastic cells but reveal interesting variations from the normal pattern of the Golgi material and mitochondria.

Certain changes can usually be recognized in a mammary gland of old mice in which a neoplastic growth develops, and a sudden morphologic change from normal to neoplastic is not found. Cystic dilatation of ducts, chronic inflammatory reactions in the interstitial tissue, and nodular hyperplasia of the mammary epithelium are usual.

The mammary tumors invade and infiltrate contiguous tissue, metastasize to the lungs and other sites, and recur after incomplete removal. The neoplasms can be transplanted into mice of the same genetic constitution, and some grow heterologously in the anterior chamber of the eye of rabbits or guinea pigs.<sup>29</sup> The tumors grow in tissue culture and can be cultivated in the yolk sac of the embryonic chick.<sup>32</sup>

The biochemical constituents of mammary tumors are on the whole very similar to those of other mouse tumors. There is an accumulation of lactic acid, a lower pH, and a higher rate of anaerobic glycolysis than in most normal tissues. The vitamin concentration is near the upper level for other tumors, and the pattern of enzymes is similar to other mouse tumors. The values for the esterase of the blood serum, the catalase activity of the liver and kidney, and the hemoglobin of the blood are lowered with growing mammary, as well as other, tumors.

Soon after the inception of cancer research on mice, it was noted that tumors appeared more often within certain cages of the colonies than within others. The immediate response to the observations of this selective occurrence of tumors was the suggestion of an infectious origin, particularly stressed by Borrel. In opposition to this theory, Loeb's studies suggested that hereditary

factors were involved, and this concept was strengthened by the experiments of several investigators. J. A. Murray's paper of 1911 presented convincing evidence that female mice, in whose immediate ancestry cancer of the breast occurred, were distinctly more liable to develop the disease than mice in whose ancestry tumors were more remote. The experiments of Lathrop and Loeb and of Slye further demonstrated that hereditary factors influenced the formation of tumors. The work, however, encountered a major obstacle because it dealt with heterogeneous stocks. In Slye's case, the lack of homozygous animals and the concept that all tumors could be grouped as a single character contributed to the misinterpretation of the results as indicating a single mendelian recessive inheritance of cancer. As early as 1909, Little foresaw that homozygous strains were essential for an adequate analysis of characters as complicated as tumors. The development of inbred strains of mice, requiring years of accurately recorded inbreeding, was one of the great contributions to cancer research. Experiments with homozygous strains of mice with incidences of mammary tumors ranging from less than 1 to over 90 per cent, developed by Little, Strong, and other geneticists, did not allow postulations of any simple genetic transmission of mammary or other tumors and also showed that different types of tumors are inherited as separate characters. At the same time, the work reiterated that genetic factors were important in the development of such tumors.

It is now established that susceptibility to mammary tumors is not a character with alternative (all-or-none) expression but is expressed in degree. Genetic factors influencing susceptibility are multiple. There is a relationship between mammary tumor development and a known, inherited, single-factor, coat-color trait, lethal yellow ( $A^y$ ).

*The Role of Hormones.*—The experimental demonstration of the influence of ovarian hormones on the development of mammary tumors in mice was begun in 1913 by the work of Loeb and his associates. Before these experiments could be started, it was necessary to establish the fact that mammary carcinoma occurred almost exclusively in females, that the incidence of mammary tumors was markedly different in different families or strains kept under similar environmental conditions, and that in each strain the rate of mammary cancer and the average age of the animals at which neoplasms appeared remained fairly stable.

It was found that mammary tumors occurred more frequently in breeding than in nonbreeding mice. In some strains, the incidence of tumors is proportional to the number of pregnancies undergone by the mice. Loeb further demonstrated that the incidence of tumors can be radically reduced by ovariectomy, and that the incidence is related to the age of the animal at the time of ovariectomy. Cori and W. S. Murray substantiated these findings, and the latter succeeded in obtaining mammary tumors in castrated male mice bearing ovarian grafts.

With the advent of chemically isolated estrogens, Lacassagne in 1932 reported the appearance of mammary tumors in male mice injected with these

compounds. The work was rapidly expanded and elaborated by numerous investigators, noteworthy contributions being made by Loeb, Lacassagne, Gardner, Burrows, and Bousser. Most important was the fact that estrogens would elicit mammary tumors in males of strains in which females developed such tumors spontaneously, and in approximately the same incidence. Males of strains in which the tumor incidence was extremely low did not develop mammary cancer no matter how strenuously they were treated with estrogens.

Development of mammary carcinomas in male mice of susceptible strains has been elicited with all the natural and synthetic estrogenic compounds that have been studied from this standpoint. The list includes estrone, estradiol, estriol, equilin, equilenin and their benzoates, diethylstilbestrol and its dipropionate, and triphenylethylene. In general, the carcinogenic activity tended to be related to the amount of estrogen in physiologic units rather than to chemical configuration or other properties. The chemicals could be administered subcutaneously, percutaneously, or orally with the same results, depending on the physiologic activity by the particular route. However, they had to be administered for some length of time, usually about eight weeks or longer, for tumors to appear at a subsequent date. With the compounds in oily or aqueous media, having short periods of activity due to rapid elimination, relatively heavy doses were required to elicit the carcinogenic reaction. When the compounds were given in the form of subcutaneously implanted pellets allowing steady and constant absorption, it was found that the dose of estrogen needed for the induction of mammary tumors was not above that physiologically elaborated by untreated female mice.

These experiments also permitted a thorough microscopic study of the changes in the breast leading to neoplasia.

In the male or the ovariectomized immature female with an intact pituitary, the mammary gland is a rudimentary structure of a few stunted ducts. The ducts begin to proliferate and to dilate within a few days after the administration of estrogens. The ducts soon form buds, and the cells of the proliferating epithelium are large, with clear cytoplasm and vesicular nuclei; an increase in mitoses is detectable by the use of colchicine. In some ducts, the cells become arranged in several layers and secrete an acidophilic product in the form of intracellular and extracellular droplets. The process progresses to the formation of small acinous lobules, so that the rudimentary breast becomes as well developed as that in the normal female. With excessive doses of estrogen, however, the glands become stunted and have localized areas of extensive alveolar development. If administration of estrogen is discontinued at this point, the mammary hyperplasia undergoes gradual regression. With continued estrogenation, there is progressive hyperplasia of the alveoli and ducts; dilation of the ducts, round-cell infiltration, and increase in periductal fibrous tissue are observed inconstantly. In mice of strains in which adenocarcinoma does not develop, the process does not progress beyond this hyperplasia. In mice that develop cancer, there is a multicentric formation of adenomatous nodules which often coalesce, and adenocarcinoma develops in these

centers. Microscopic examination does not reveal any sudden alteration which may be designated as the point at which the normal cells become neoplastic. The site, the growth, and the histologic appearance of mammary tumors elicited in mice injected with estrogens correspond in all details to the description of the spontaneous adenocarcinomas in female mice.

Numerous investigations have been performed in an attempt to discover differences in the morphology or physiology of the breast in mice belonging to strains with different incidences of mammary carcinoma. No clear differences in morphology have been established. In general, however, hyperplasia of the ducts and alveoli under the stimulation of estrogens tends to be more rapid and more uneven, with the eventual development of adenomatous nodules, in the high-mammary-tumor strains. Distention of the ducts into cysts, round-cell infiltration, and an increase in periductal fibrous tissue are inconsistent features apparently not associated with the eventual development of mammary neoplasia.

The morphologic studies also stress that the essential difference between male and female mice, as far as the appearance of mammary carcinoma is concerned, is the practical absence of the mammary gland in the male animals. The formation of the gland and the increase in cellular elements under the stimulation of estrogens thus exteriorize or make possible the development of some factor already present in the animal that leads to the eventual appearance of gross mammary tumors. It is also clear that something more than excess growth is operating in the cancerous transformation of the breast. The onset of recognizable malignant nodules occurs in breeding females or in mice injected previously with estrogens when the major part of the mammary gland is involuting. A difference between the normal growth process and the neoplastic process is also indicated by the unsuccessful attempts to produce a direct transition of the fully developed mammary gland of pregnancy or lactation into a carcinomatous gland by continued injections of large doses of estrogen.

Studies aimed at demonstrating the essential difference between strains of mice that are susceptible to mammary carcinogenesis and those that are not, either spontaneously or under the influence of exogenously supplied estrogens, also took other lines. The estrus cycle of mice of different strains was compared; no correlation was found between the length or regularity of the sexual cycle, duration of keratinization of vaginal mucosa, and the occurrence of tumors. The susceptibility of mice to estrogens, as manifested by the dose required to produce estrus in spayed mice, was not correlated with the susceptibility. The urinary excretion of estrogens and 17-ketosteroids<sup>41</sup> and the ability of the liver to destroy estradiol *in vitro* do not differ significantly in the low- and the high-mammary-tumor strains. Nor could correlation be established with degenerative changes in the adrenals, the pituitary, or other endocrine organs.

Although the estrogens maintained their focal point in the genesis of mammary tumors in mice, it was shown that other endocrine secretions, especially

those of the adrenal cortex and the anterior pituitary, were involved. Progesterone is reported to reduce the incidence of mammary tumors in susceptible mice.<sup>35</sup> Androgens, given over protracted periods of time, reduce the incidence of such tumors. The action is probably analogous to castration, since androgens suppress the estrus cycle and prevent follicular maturation. The adrenal cortex, in relation to sexual functions, can be considered as a potentially bisexual accessory gland capable of secreting either estrogens or androgens under the influence of stimuli from the pituitary gland. Woolley demonstrated that gonadectomy of young mice of two high-tumor strains led to progressive hyperplasia of the adrenal cortex. There was gradual recovery of the uterus, vagina, and breast from the castrate state, and mammary tumors developed in the females. One male castrated at birth also developed a mammary tumor. In strains that do not develop mammary tumors spontaneously, no mammary tumors were obtained.<sup>67</sup> Mammary carcinogenesis following gonadectomy is probably best explained by the extragenital production of estrogens in the hyperplastic adrenocortical tissue and is dependent upon whether the normal females of the strains under consideration develop tumors of the breast. The origin of estrogens in the adrenals was supported by the close morphologic similarity of the cells of the adrenal nodules to luteinlike cells of the ovary.

The lack of pure anterior pituitary hormones has limited the work on the role of these hormones on mammary carcinogenesis. It has been shown, however, that subcutaneous graft of the hypophysis raises the incidence of mammary tumors in intact females but does not elicit them in males or ovariectomized females. Thus, the pituitary probably stimulates secretion from the ovary; it does not increase the incidence of tumors in strains of mice that do not develop such tumors spontaneously.

It has been indicated that, although various alterations in the hormonal balance of the animal reflect in changed incidence of mammary tumors, the attempts to correlate the degree of genetic or hormonal predisposition to mammary cancer with various physiologic and morphologic manifestations remained unsuccessful. Mice of strains in which the mammary tumor incidence was practically nil did not develop such tumors despite radical estrogenation or other procedures.

The essential difference between mice resistant to mammary carcinogenesis and mice of susceptible strains remained obscure. Much of the clarification was due to investigations in the inheritance of these tumors, which revealed an extrachromosomal factor that was involved.

*The Extrachromosomal Factor.*—Between 1930 and 1933 the members of the staff of the Roscoe B. Jackson Memorial Laboratory conducted a number of reciprocal hybridization experiments with the high- and low-tumor strains that they had by that time perfected. The results of these experiments, along with these of Korteweg, of Holland, led to the discovery of the extrachromosomal factor in mammary-tumor development and opened the door to one of the most fruitful lines of cancer research of the past decade. The discovery was that the hybrid female offspring resulting from the mating of high-tumor-

strain females to low-tumor-strain males developed tumors in approximately the same incidence as that of the high-tumor strain; but when the reciprocal cross was made, that is, low-tumor-strain females times high-tumor-strain males, the tumor incidence of the female offspring was but little greater than that of the low-tumor strain. Thus, the incidence of the  $F_1$  generation approximated that of the maternal strain.

The Jackson Laboratory group conducted four different experiments including the reciprocal crosses between seven low- and high-tumor strains of mice. The results in all four experiments, entailing a total of 532  $F_1$  females, were consistent in showing that the tumor incidence of the  $F_1$  females resembled that of the strain of the mother. One cross was carried to the  $F_2$  generation, and it was found that the difference between the reciprocal  $F_1$  hybrids was carried on into the  $F_2$  generation. This generation included a total of 1,139 females, and hence the results were conclusive. However, eight generations of repeated backcrosses of the mice to the low-tumor strain males, thus building up the genetic background of the resistant mice for the extrachromosomal factor, eliminated the extrachromosomal influence and revealed the importance of genetic susceptibility.

Since the genetic constitution even including the sex chromosomes had to be considered the same for the two groups of females resulting from reciprocal crosses between two isogenic lines, it was obvious that this effect was not transmitted through the chromosomes. It had to be some extrachromosomal factor which the female was capable of transmitting to her offspring. It appeared that this factor was likely transmitted by one of three possible routes. It might be transmitted through the cytoplasm of the egg, cytoplasmic inheritance; it might be transmitted through the placenta, an intrauterine influence; or it might be transmitted through the milk, a milk influence.

Bittner undertook the study of the third possibility, the foster nursing problem, and it was through his work that the factor was primarily revealed.

Almost astonishing in its simplicity, the transfer of mice of high-mammary-tumor strains shortly after their birth to foster mothers of low-mammary-tumor strains reduced the occurrence of neoplasms. The low incidence was maintained in subsequent generations; in two strains with a previous incidence of 80 per cent, animals of the tenth to the twentieth generation after a single interruption of the ingestion of milk from their mothers of high-cancer strain had an incidence of less than 2 per cent. When complete interruption of the milk ingestion could be assured, as by removal of the young from the uterus, even a lower residual rate of tumors was encountered. The basic observation has now been repeated and substantiated in one dozen or more independent laboratories throughout the world.

When low-tumor strains of mice are suckled by foster mothers of high-mammary-tumor strains, there is an increase in the incidence of mammary tumors. Whether this increased incidence is maintained or not depends on the genetic susceptibility of the strain. Strain C mice, possessing this genetic susceptibility and having less than 2 per cent incidence of mammary tumors,



were transformed, after nursing on high-mammary-tumor strain foster mothers, into a line having an incidence of over 80 per cent of tumors in the  $F_2$  to the  $F_{11}$  generations. In contrast, in mice of strain C57 black, having a high genetic resistance to mammary tumors and the milk agent, the incidence may be increased to as high as 75 per cent by foster nursing them on animals possessing the milk agent,<sup>31</sup> yet in subsequent generations the incidence rapidly decreases as the genetic resistance overcomes the milk influence. Appropriate tests show that these resistant mice lose their ability to transmit or propagate the milk influence to mice of other strains subsequently nursed by them.<sup>3</sup>

It was also established, in at least four independent laboratories, that the induction of mammary tumors in male mice injected with estrogens was also dependent upon whether such animals possessed or did not possess the milk influence. Thus, the agent in the milk is ineffective in the absence of hormonal stimulation of the breast.

Despite the lack of an adequate, rapid bio-assay technique, so that twelve months or longer are required for any particular determination, and despite the lack of stable preparations of the milk agent, depriving the experimenter of a standard sample of reference, much has been learned concerning the nature and properties of the milk agent during the past six years. Most of these contributions have been made by Bittner and his group and by the workers at the National Cancer Institute.

It is known that the agent is present in the milk of high-mammary-tumor strains throughout the period of lactation, although it may vary in concentration during the reproductive period of the mouse. When the young of a high-tumor strain remain with their mothers for varying periods before being foster nursed by resistant-strain females, the young remaining with their mothers for shorter periods develop fewer tumors at a later average age than do the young permitted to nurse from their mothers for longer periods. Other work, in which measured amounts of milk from high-tumor-strain females were fed to susceptible young by means of stomach tube, confirmed this dose-response relationship. A single oral administration of 0.1 c.c. of high-tumor-strain milk to susceptible young mice produced mammary tumors in over 90 per cent of the animals, some eight months later. Evidently there occurs an event in the first few hours of life which leads to the appearance of mammary cancer months later.

The intraperitoneal route of administration of the milk agent is more efficacious than the oral route. In all experiments with the agent, mammary tumors do not appear with any greater frequency at, or near, the site of injection than in other mammary glands of the animals.

The agent is widely distributed throughout the body of the mouse. Tumors have been produced in susceptible mice following subcutaneous implantation of pieces of spleen,<sup>14</sup> lactating mammary gland, and subcutaneous injection of whole blood. The injection of serum of mice has produced a low incidence of mammary tumors whereas a high incidence has been obtained in mice injected with the total cell suspensions of the blood. This fact suggests that the agent is associated with the cellular elements. Extracts of mammary tumors fed to

susceptible mice evoke tumors, a finding demonstrating the presence of the agent in the tumor tissue. Apparently the agent does not penetrate through the placenta. Despite its wide distribution throughout the body, the milk agent is apparently not contagious through body contact.

Adult mice are more resistant to the milk agent than are those up to six weeks of age.<sup>5</sup> There are pronounced differences in degrees of genetic susceptibility of different strains of mice to the milk agent, and the ability of such strains to transmit the agent.<sup>35</sup> Probably the activity of the milk agent differs in some of the strains. The milk influence does not affect the genetic make-up of the mouse in relation to the development of mammary tumors.

Material obtained from lactating mammary tissue of high-tumor-strain mice by filtration through Seitz filters is capable of giving rise to mammary tumors in other mice. Desiccation of lactating mammary gland tissue at room temperature resulted in great loss of activity within one week. Extracts of mammary-tumor tissue to which 50 per cent glycerin was added at 8° C. retained activity for nine days, but were inactive eighty days after the procedure. Lyophilized mammary-tumor tissue suspended in water and fed to mice produced tumors. The preparation was still active when tested six months after lyophilization, although the comparative potency with the original material was not determined, but it was inactive one year following the procedure. The agent survived in mammary tumors propagated in the yolk sac of chicken eggs.<sup>10</sup>

The agent is destroyed in mouse milk heated to 61 or 66° C. for thirty minutes and in fresh mammary tumor extracts heated to 56 or 66° for thirty minutes. It survives in mouse milk kept at 8° C. for fourteen days, is active in extracts of mammary tumors at p<sub>H</sub> 5.5 to 10.2, but is inactive at p<sub>H</sub> 4.5. It is not inactivated by acetone or petroleum ether.<sup>8</sup>

Ultracentrifugation experiments showed that the agent when obtained from lactating mammary glands and suspended in distilled water was sedimented at 110,000 times gravity for one hour. Extension of the ultracentrifuge studies revealed that there were two principal components for the active tumor extract, which when extrapolated to zero concentration were 62 S and 90-92 S. However, somewhat similar components were found in the milk of strains of mice with low incidence of spontaneous mammary tumors, as well as in human mammary carcinoma and chick embryo. A minimum molecular weight of three to four million was estimated for the macromolecular material of 62 S, while the faster moving component had a molecular weight of at least five million. The variations of sedimentation rate with concentration indicated an asymmetric particle.

Ultraviolet absorption spectrograms and other tests indicated the presence of a ribose-nucleic acid complex in the material from mammary tumors containing the agent. However, since similar components were present in normal tissues, it is not clear whether the agent inciting mammary tumors in mice is an altered ribose-nucleic acid complex or whether this complex is merely the carrier of the active agent associated with it.

Rabbit serum obtained following injections of saline extract of mammary tumor or with ultracentrifuge pellet material neutralized fresh mouse mammary-tumor extracts in vitro. Intraperitoneal injections of immune rabbit sera protected susceptible mice against the development of mammary tumors following the feeding of active fresh tumor extract.<sup>6</sup>

Filtration and ultracentrifugation experiments show that the milk agent can be transmitted by cell-free material, and its transmission through many generations of mice implies propagation. These features suggest the action of an agent belonging to or related to the viruses.

It is similar to known tumor viruses in its specificity for a certain tissue. It is apparently not involved in the genesis of spontaneous pulmonary or hepatic tumors, of bone tumors,<sup>47, 48</sup> or of induced tumors of the lung, subcutaneous tissues, testes, uterus, or the pituitary.

Unsuccessful attempts to transmit the mouse milk agent to deer mice (*Peromyscus*) suggest that the agent, in common with known tumor viruses possesses a degree of specificity; and if a similar factor is active in the occurrence of breast cancer in other species, conclusive tests for its presence must be performed in animals of the same species.

It is not known whether the milk agent continues indefinitely in propagable tumors and whether its presence is required for the continued growth of such transplanted tumors. Preliminary investigations indicate that the presence of the milk agent is not necessary for the propagation of an established tumor, unless a latent phase is postulated.

The mouse mammary-tumor influence differs from known tumor viruses in its relatively long latent period. A mouse ingesting milk shortly after birth will develop a neoplasm six to twenty-four months later. Tumor development is not necessary for transmission of the influence from mother or foster mother to offspring; in fact, under ordinary conditions the causal agent is transferred in the absence of recognized tumor, and this transfer continues for many generations. In this respect, the milk agent acts as a latent virus infection.

Up to the present time, no changes in the organism have been described following the introduction of the milk agent. The mice are not sick and gain in weight equally, as compared with animals without the milk influence. The onset of the estrus cycles and the character of the cycles for the first three months are unaltered. The adrenal changes following estrogen administrations or castration are not influenced by the presence or absence of the milk agent. The agent does not produce consistent and clear-cut alteration of the architecture of the mammary gland.

*Other Factors in the Genesis of Mammary Tumors in Mice.*—The current concept of the etiology of mammary tumors in mice, as expressed by Bittner, is that at least three factors must be present for their development (1) an inherited susceptibility, (2) hormonal stimulation, and (3) an active agent that is generally transmitted through the milk. All three factors must be present for the genesis of mammary carcinoma. Thus, unless the milk agent is intro-

duced into strains of mice possessing genetic susceptibility (such as strain C), large doses of estrogen do not lead to development of mammary neoplasia. Male mice do not develop tumors of the breast despite the presence of genetic susceptibility or the milk influence unless the lacking hormonal factor is supplied. On the other hand, a quantitative deficiency of any one factor probably can be overcome by the relative quantitative increase in the other two factors. Thus, the relative genetic resistance to mammary tumors in mice of strain C57 black can be overcome by the introduction of the milk factor and sufficient hormonal stimulation.

These three sets of factors, however, by no means exhaust the number of influences that may play a role in the genesis of these tumors. Of these, nutrition has received the greatest attention. Underfeeding of the total balanced diet or of certain essential constituents thereof, such as sulfur-containing amino acids, reduces the occurrence of mammary tumors.

The mere reduction of a balanced ad libitum diet by one-third led to the total suppression of mammary tumors in a highly susceptible strain possessing the milk agent.<sup>40</sup> The mechanism is probably the production of pituitary insufficiency which leads to a lowered level of ovarian secretion and a relative refractoriness of the mammary gland to estrogenic substances. It is known that mice deprived of cysteine in the diet have but few and irregular estrus cycles. It is not known whether diet or other environmental factors influence the transmission and otherwise modify the action of the milk agent, but this does not appear unlikely.

It has been reported that the incidence of mammary tumors is increased and the average tumor age is decreased in mice kept at an environmental temperature of 68° F. as compared with mice living at a temperature of 91° F.<sup>61</sup> Even such mild environmental changes as crowding or isolating animals are reflected in the incidence and time of appearance of mammary tumors, probably because of the effect of these factors on food consumption and the estrus cycle.

Furthermore, data have been accumulating to the effect that not all mammary tumors in mice are associated with or due to the presence of the milk agent. Perhaps the most striking demonstrations have been with animals injected with methylcholanthrene, a polycyclic hydrocarbon that elicits a variety of tumors in mice at the site of introduction (such as subcutaneous sarcoma or cutaneous carcinoma) and at distant sites (such as pulmonary tumors).

In 1939 it was shown that painting of methylcholanthrene on the skin of breeding female mice of a strain that is known to possess the milk agent and genetic susceptibility to mammary tumors (strain dba) accelerated the appearance of mammary tumors. This observation was subsequently repeated in two other laboratories, using the same strain of mice. Mammary tumors were not obtained in male mice, nor was the time of appearance of tumors accelerated in nonbreeding mice. Recently mammary tumors have been elicited by percutaneously administered methylcholanthrene in crosses of two genetically susceptible strains deprived of the milk agent.<sup>42</sup>

animals, the longer life span, and the lower incidence of tumors, all resulting in greater expense, have been important factors in limiting the advances.

*Rats.*—The incidence of spontaneous mammary tumors in the rat is low, and the tumors that occur are usually fibroepithelial growths, designated as benign fibroadenomas. Curtis and associates<sup>12</sup> stated that fibroadenomas occurred in 0.9 per cent of the females that survived fourteen months or longer. The incidence for the Rockland colony of rats was 0.8 per cent,<sup>36</sup> and estimates in other colonies were up to 8.0 per cent.<sup>11</sup>

Fibroadenomas of spontaneous origin are transplantable into rats of the same genetic constitution and usually grow progressively to large size.<sup>18</sup> The proportion between the fibrous and the epithelial elements is variable and can be modified by the sex of the host animal or by the administration of hormones. The tumors are more fibrous and grow more slowly in the presence of androgens, and are more epithelial and grow faster in the presence of estrogens.<sup>33, 34, 49, 50</sup> Papillary cysts are encountered occasionally in these tumors. Upon serial transplantation, sarcomatous changes may take place.<sup>36</sup>

Wolfe and his co-workers<sup>11, 63, 64, 66</sup> have studied a colony of rats at Albany (AS strain) characterized by a relatively high incidence of spontaneous mammary tumors. Of 1,827 females surviving for five months or longer, 186 developed tumors at an average age of fifteen months. The animals were not homozygous, and in one line eighteen tumors appeared among eighty females. A study of 149 tumors showed 122 fibroadenomas, 10 fibromas, 11 adenomas, 5 cystadenomas, and 1 carcinoma. The rats of this colony revealed a number of abnormalities which were probably endocrine in character and strongly suggested anterior pituitary deficiency. The estrus cycles were abnormal, fertility was diminished in both males and females, growth was deficient, and prolonged gestation and fetal resorption occurred in a high percentage of the females. Bio-assays of the tumor tissue for estrogen were negative, permitting a supposition that hyperestrinism is not the sole factor in the development of these tumors.

It is not known whether repeated gestations increase the incidence of fibroadenomas in rats. Bagg and Jacksen<sup>7</sup> reported one tumor in a Wistar strain rat that had eleven litters, but no other tumors were encountered in fifty-six breeding females or ten other controls.

Mammary carcinoma of spontaneous origin in the rat is rare, occurring in 0.02 per cent of the females observed by Curtis and co-workers<sup>12</sup> and in 0.05 per cent of the Albany strain. However, mammary carcinoma has been induced consistently with the prolonged administration of estrogens in at least three laboratories.

Geschickter<sup>21-24</sup> used albino rats that had been inbred for seven years. In a colony of over 5,000 animals, no mammary cancer was seen, and less than two per cent developed fibroadenomas at an average age of over eighteen months. Of 555 rats injected with estrogens, 202 developed carcinoma of the breast, although in only 2 cases were metastases present. The author described all stages of development of these tumors from hyperplasia of the ducts and lobules to frank carcinoma. The same morphologic alterations were found in

the breasts of mice under estrogen administrations, with the exception of the pronounced fibrous reaction. In the mouse, increase in periductal fibrous tissue is relatively slight, whereas in the rat the fibrosis is a more striking feature than epithelial proliferation, with formation of fibroadenomas. It is not entirely certain that these estrogen-induced fibroadenomas are identical with the spontaneous tumors, since the induced tumors usually become stationary in size or regress upon cessation of estrogenation<sup>56, 57</sup> and have not been transplanted successfully. The spontaneous tumors usually grow progressively and are transplantable.

The investigations of Geschickter are somewhat confusing because parallels are constantly drawn to human pathology and because an impression may be gathered that the types of lesions obtained can be readily controlled by modifications in the type and amount of the hormone administrations. As in mice, the incidence of mammary cancer is increased and the average tumor age is decreased proportionately with the dose of the estrogen. The estrogens must be given continuously for a period of several months, and slow constant absorption from subcutaneously implanted pellets is more efficacious in eliciting cancer than are intermittent injections of the hormones in oily solutions. The carcinogenic activity of different chemicals with estrogenic activity is related to its physiologic potency and duration of effect rather than to chemical structure or other properties. To produce mammary cancer in the rat, it is apparently necessary to expose the animal to ten or more times the physiologic amount of estrogens. This is probably correct, in contrast with the situation in mice; if only the physiologically elaborated amounts were needed, normal breeding female rats would have a much higher incidence of spontaneous cancer of the breast. Geschickter described eight female rats that developed mammary cancer in twenty-one to sixty days following the implantation of multiple pellets of estrone, estradiol, or diethylstilbestrol. This is considerably faster than the earliest appearance of mammary tumors in mice, in which eighty-four days is the shortest recorded latent period. Sex, age, or castration were stated to have little effect on susceptibility to estrogen-induced mammary cancer, although senile animals were more susceptible. The latter point is at variance with similar studies on mice.<sup>45</sup>

Nelson<sup>55</sup> using rats of the Long-Evans hooded strain, in which only 4 fibroadenomas had been seen in fifteen years, reported the induction of 68 carcinomas of the breast in 103 animals. The rats received daily injections of 50 gamma of diethylstilbestrol, or subcutaneously implanted pellets of diethylstilbestrol or estrone. Metastases were present in thirty-three rats. The tumors were classified as: duct carcinoma, thirteen; adenocarcinoma, eight; duct and adenocarcinoma, thirteen; and carcinoma simplex, five. Male and female rats were equally susceptible to the induction of tumors. Eisen<sup>17</sup> obtained two cancers of the breast in fifty-four rats of the Sherman strain implanted with estradiol dipropionate in paraffin.

Dunning and Curtis<sup>16</sup> implanted pellets of diethylstilbestrol in cholesterol into rats of three inbred strains. Mammary cancer developed in 80 per cent

of the animals of one of the strains. Rats of another strain have shown no cancer of the breast after twelve to fourteen months. Reciprocal hybrids between these two strains are being tested for the possible transmission of a milk factor analogous to the milk factor observed in the etiology of mouse mammary tumors.

Wilson and associates<sup>62</sup> reported the induction of mammary tumors in rats with 2-acetylaminofluorene, a nonestrogenic chemical used as an insecticide. The incorporation of the compound in the diet at a concentration of 0.03 per cent or higher for at least ninety-five days led to the appearance of a variety of tumors, especially hepatoma and carcinoma of the urinary bladder, and including three mammary adenocarcinomas in thirty-nine rats. The observation was confirmed by Bielschowsky.<sup>6</sup> Wistar rats were fed 2-acetylaminofluorene, 4 mg. daily for thirty weeks; of thirty-six females, twenty-three developed mammary cancer, and of forty-one males, three developed mammary cancer. It was stated that cancer of the breast could be produced in this strain of rat also by the subcutaneous implantation of diethylstilbestrol pellets.

*Rabbits.*—Very few cases of spontaneous tumors of the breast of rabbits have been recorded in the literature. Greene<sup>25-28</sup> published a detailed description of a family of rabbits under his observation in which twenty-nine had mammary abnormalities at an average age of 30 months. Eleven rabbits developed frank carcinoma after an average period of 15 months; metastases were found in five cases.

The first indication of mammary disorder in twenty-five animals was a sudden engorgement of all the mammary tissue, so that the glands consisted of large thin-walled cysts. This usually occurred following an infertile mating or estrus period. A slight glandular enlargement in more localized areas sometimes took place unassociated with reproductive activity. The engorgement usually persisted for several weeks and then subsided rather suddenly. Recurrences of the condition finally led to a persistence of small, bluish cysts filled with brown fluid. These cystic areas gradually became firm, and occasionally bloody fluid could be expressed from the nipple. Tumors arose as papillomatous outgrowths from the epithelial lining of dilated acini and duct; these grew continuously, anastomosed with others, and formed acinuslike structures. Invasion of surrounding tissues was next observed, and the cells appeared in adenomatous masses or in solid medullary sheets. The connective tissue response sometimes converted the entire breast into a scirrhus type of growth. Retraction of the nipple, fixation to the skin and muscle, and external ulceration were frequently observed. The duration of life after the appearance of invasion varied from six to forty-eight weeks.

In four rabbits, there was no antecedent mammary engorgement. The tumors appeared as solitary nodules in normal breast tissue and consisted of masses of proliferations of acini. Three of these adenomas progressed within twelve to sixteen months to adenocarcinomas.

Analysis of the factors concerned in the genesis of these tumors showed that the tumors occurred almost exclusively in two family groups of rabbits.

Animals of unrelated lines were foster nursed by tumor-bearing rabbits, but no instance of mammary tumors developed. This is evidence against the presence of a milk-transmissible factor.

Fertility was reduced during the period of mammary disorder in almost all the affected animals; five were completely sterile. The average number of progeny was reduced, and the numbers of resorptions of products of conception and of young born dead in litters were increased.

The pituitary was enlarged in all stages of the disease, but not in rabbits which developed tumors without antecedent mammary abnormality. The pituitary enlargement was due to chromophobe hyperplasia. The endometrium of the uterus was hyperplastic and cystic, and in both groups of rabbits the ovaries frequently contained cysts. The endocrine changes were comparable with those found in animals after long-continued administration of estrogenic substances. It was inferred that the neoplasms represented a natural counterpart of the experimental induction of tumors with estrogens.

Geschickter<sup>22</sup> injected an unstated number of castrated rabbits with daily doses of 0.5 or 1.0 mg. of dimethylstilbestrol. Three rabbits developed papillary cystadenoma of the breast in ten to fifteen months, and in one this progressed to carcinoma at twenty months.

*Dogs.*—Mammary cancer is one of the commoner forms of canine neoplasia, and the incidence is relatively high in old females.<sup>52, 53</sup> With two exceptions in which dogs with mammary tumors were used for experiments in therapy, publications on this subject have dealt exclusively with morphologic aspects of the neoplasms. Recently, Huggins and Moulder<sup>39</sup> have applied this material to more extensive experimentation.

Most of the neoplasms are mixed tumors containing in addition to neoplastic epithelium, at times, myxomatous tissue, cartilage, osteoid tissue, and bone. The tumors are formed of multiple nodules which may be firm or cystic, and although these nodules are usually well encapsulated and discrete, the skin is sometimes invaded. All breasts may be involved, but the mammary glands of the inguinal region are the most common site. The histologic picture of the epithelium varies in arrangement from small acini to large cysts containing papillary processes. Metastases are found in the regional lymph nodes and in the lungs, usually in the form of papillary carcinomatous cysts. This tissue in transplants to abdominal connective tissue stimulated local bone formation.<sup>39</sup>

Huggins and Moulder studied 120 mammary tumors in 31 dogs. Metastases were present in 4 dogs. All the dogs also had tumors of the adrenal cortex made up of cells which resembled the cells of the zona fasciculata. The adrenal tumors were not confined to females with mammary cancer but were found often in other old dogs, both male and female. The anterior pituitary was usually large in females with tumors.

In nineteen dogs, fluid could be expressed from the nipple overlying a mammary tumor. Solids, fats, calcium, and citric acid were decreased, and the chlorides and alkaline phosphatases were increased in this fluid in comparison with normal milk of dogs. Ovariectomy and adrenalectomy of dogs with tumors did not suppress mammary secretion for prolonged periods.



The importance of the use of the dog in experiments on mammary carcinogenesis needs emphasis because previous studies have been limited to rodents. Inbreeding of dogs in order that homozygous strains may become available has been commenced at the Roscoe B. Jackson Memorial Laboratory.

*Guinea Pigs and Monkeys.*—There are no reports on the induction of mammary carcinoma in guinea pigs or in monkeys. In reviews of his extensive work on the hormonal induction and suppression of fibroids in guinea pigs, Lipschütz<sup>43, 44</sup> stated that adenofibroma of the breast has rarely been produced but that no carcinomas have been seen.

Three laboratories have injected rhesus monkeys with estrogens for protracted periods without induction of neoplastic changes in the breast. At Yale,<sup>1</sup> in experiments begun in 1930, six monkeys have survived several years' intensive treatment with estrogenic hormones in high doses. Folley and co-workers<sup>20</sup> reported that no carcinomatous changes were observed in the mammary glands of six monkeys which were injected daily with estrone either continuously or for the major part of periods varying between one and three years. Geschickter<sup>23</sup> has maintained six monkeys on continuous injection of estrone or estradiol for over three years without neoplastic effects.

#### POSSIBLE IMPLICATIONS FOR MAN

It is tempting to speculate how far the experimental findings on animals extend to the genesis of mammary tumors in man. A considerable number of papers drawing such parallels and deductions have appeared in the literature, and reference to man has characterized the publications of a few laboratory investigators. In view of the evident differences in the factors that lead to mammary neoplasia in mice, in rats, and in rabbits, any but the most tentative extrapolations to man must be regarded as unwarranted.

The study of factors that may be of etiologic significance in the occurrence of mammary cancer in man has been based necessarily on statistics. It is well to realize the disadvantages of this approach. The reliability of any data based on histories of cases is always dubious because it extends over such long periods, because of the incipient early symptoms of the disease, and because the attention drawn to the breast in women with tumors of the breast, with its resultant stimulus for remembrance and possible misinterpretations, is absent in the usual control groups of women that may otherwise be carefully selected for comparison. Furthermore, it is too often forgotten that statistical correlation does not imply causal or other direct connection.

There is some evidence that there are significant differences in the incidence of mammary cancer in different populations. This is particularly striking in the low incidence of mammary cancer in Japanese as compared with European women. There is also a predominance of mammary cancer in the ancestry of women with such tumors. Perhaps the most impressive data have been presented by Martynova in Russia, Waaler in Norway, and Wassink in Holland.\* Added to the statistically recorded preponderance of mammary can-

\*Undesignated references in this section are to be found in the paper by Shimkin.<sup>49</sup>

cer in families of patients with mammary cancer are occasional striking family histories, including simultaneous occurrence of mammary cancer in homologous twins. Whether these cases are coincidences in a relatively common disease, or whether these occurrences have actual significance is not entirely established.

The difficulties encountered in the compilation and evaluation of data on the familial occurrence of mammary cancer in man may be gaged by the extensive work that had to be performed before similar findings were made on noninbred mice. It took three generations, all under continual control and observation, to establish that cancerous ancestry increased the incidence of mammary tumors in the mice colony of J. A. Murray. In rats and rabbits, as well as mice, familial occurrence of mammary tumors has been a striking feature. Such familial occurrence, although necessarily involving hereditary susceptibility, may be due to common environmental conditions, habits, or some transmissible agents or factors.

Mammary cancer occurs but rarely in the male of any species. In man, the comparative incidence with females is in the neighborhood of 1 to 96. This may be attributed to the absence of stimulation by ovarian hormones in the males. It implies that the male breast is a rudimentary organ, and cancer of the breast cannot develop when there is practically no breast. The direct relationship, therefore, is between hormones and mammary development and not necessarily between hormones and mammary cancer.<sup>30, 54</sup>

There is no evidence in the literature that proves that even heavy and protracted use of estrogenic substances has been instrumental in producing mammary carcinoma in women. If parallels are to be drawn between experiments on animals and the danger of the compounds in clinical use, it would have to be decided whether man most closely resembles the mouse, in which mammary tumors are elicited with physiologic doses, the rat, in which the carcinogenic dose is apparently considerably above the physiologic limit, or the guinea pig or monkey, in which carcinomas have not been elicited. Nevertheless, the possibility of carcinogenesis with the heavy, protracted use of these agents cannot be neglected, although of even greater importance is the danger of using such preparations for the treatment of breast masses which are clinically diagnosed as benign, thus leading to procrastination in surgical intervention for possible early carcinoma.

Hormonal stimuli are so essentially involved in all phases of development and function of the breast that it is impossible to dissociate them from the process of mammary carcinogenesis. There is no impressive evidence that the hormonal complex has to be abnormal for the genesis of mammary tumors in mice. On the other hand, it is suggestive that mammary tumors in rabbits are often associated with manifestations of hyperestrinism, and adenofibromas of the breast occur in the Albany strain of rats which show signs of hypopituitarism. In all species that develop mammary tumors sufficiently radical alterations induced in the hormonal balance will undoubtedly be reflected in changes in the incidence and time of appearance of the tumors.

A considerable number of statistical and more direct studies have attempted to ascertain whether hormonal abnormalities are associated with the oc-

currence of mammary cancer in man. No significant differences have been encountered in the histories of the menstrual periods of women with breast cancer as compared with normal women, and investigations of the menstrual cycles of younger women with mammary cancer have yielded no striking observations. Cytologic studies of the pituitary gland of women with mammary cancer showed no deviation from normal. In these respects, the data are similar to the observations on mice.

It has been noted repeatedly that cancer of the breast is more common in the unmarried and nulliparous women than in women who have borne children. Dorn indicated that the incidence is highest in married women without children and concluded that many of these women may be involuntarily sterile. The impression that low fertility in women is associated with a higher incidence of mammary carcinoma is further substantiated by a smaller average number of pregnancies and viable children and a higher percentage of miscarriages in women who develop breast cancer. In this regard, the data on man recall the observations on the Albany strain of rats.

The relation of possible hormonal disturbances to mammary cancer in man has been studied more directly by analyses of urinary excretion of hormones and related substances. Most investigators have concluded that the excretion of estrogens and androgens and other steroids is not abnormal in the presence of cancer of the breast. Recent work at the Memorial Hospital in New York, however, suggests changed quantitative relationship of ketosteroid compounds, probably of adrenocortical origin, in the urine of patients with mammary cancer. The frequent occurrence of adrenocortical tumors in dogs with mammary tumors and in castrated mice is brought to mind. There is yet no clinical evidence, however, of any specific endocrine dysfunction as the cause of mammary cancer in man.

The contention that nonlactation is an important factor in the genesis of mammary cancer, particularly stressed by Adair on the basis of statistics on man and by Bagg on the basis of experimental work on mice, is not impressive. It is probably true that mammary cancer is more frequent among women who do not suckle their children than among women who do. This may be evidence of a previous inflammatory state or a physiologic deficiency, possibly connected with a predisposition to neoplastic growth, rather than of carcinogenic potentialities of retained or inspissated secretions. Certainly in the mouse, nonlactation per se has little if any direct etiologic relationship to carcinogenesis.

Many clinicians and statisticians have stressed the importance of previous disturbances of the breast in the etiology of mammary cancer in man. Lane-Clayton found significant correlation between the presence of mammary cancer and an antecedent history of nonsuppurative mastitis and structural or functional abnormalities; no significant correlation was elicited in the occurrence of suppurative mastitis, cracked nipples, and trouble with the breast in connection with menstruation. Perhaps as an index of the low reliability of such data, the highest correlation in this series was obtained between external trauma to the breast and subsequent development of cancer in that breast.

An impressive number of authors have subscribed to and developed the view that cystic disease and other benign masses of the breast in women increases the calculated risk of developing carcinoma. From the standpoint of experimental work on animals, this is fully corroborated. In mice, rats, and most of the rabbits, no sharp delineation can be made histologically between normal physiologic hyperplasia, various cystic, adenomatous and papillary abnormalities, and frank malignant growth. In mice the tumors arise as small, compact, adenomatous nodules which progress gradually and continuously into invasive, metastasizing neoplasms; cystic dilatation of the ducts or lobules is of inconstant relationship to neoplasia. In most rabbits, the carcinomas arise as papillary growths in mammary cysts, so that cystic disease is a direct precursor of neoplasia. Whether these processes are continuous, that is, represent different stages of one reaction, or whether some of them represent terminal and separate end results is of course unknown, and decision cannot be made on histologic grounds.

Comparable with the morphologic observations, studies on the physiologic function show a gradual transition from the normal breast to the frankly neoplastic. Hormones, particularly the estrogens, are essential for the development, preservation, and normal function of the epithelium of the normal mammary gland. Tumors of the mammary gland are also dependent upon hormones at least to the extent that the normal tissue from which the tumors must arise is under the control of the hormones. Chronic cystic mastitis and fibroadenoma in women are apparently connected with or depend upon existent ovarian function, although, as Taylor stated, analysis of clinical histories, as well as the estimation of estrogen and prolan in the urine, has not to the present time proved that these conditions are due to any simple excess or lack of estrogenic or gonadotrophic hormone. However, both chronic cystic mastitis and fibroadenoma respond to hormonal stimuli incident to pregnancy and to menopause. Fibroadenoma of the rat is also markedly influenced by hormones. With fully established carcinoma, only a moderate reaction to hormonal stimuli is occasionally noted in some cases. The breaking away of the epithelium from normal hormonal control may be stated as one of the manifestations of the gradually acquired autonomy of the cells.

It is abundantly clear that in all species, carcinoma of the mammary gland is the end result of an intricate, prolonged interaction and combination of at least several factors or complexes of factors. In all species, a degree of genetic susceptibility and a degree of hormonal stimulation are essential, and the process can be modified by numerous secondary influences of internal and external environment. In mice a most important contribution has been made by the discovery of the transmissible milk factor which is necessary before the alteration can proceed beyond the stage of cystic or other hyperplasia. It is not known whether a similar factor is operative in rats, rabbits, or other species. In fact, data are accumulating that suggest it is not essential for the development of all mammary cancers of even the mouse, although the findings by no means eliminate the possibility if latent forms of the agent are postulated.

It is quite possible that similar agents, perhaps in closer symbiosis with the cells and not transmissible in the milk but by intrauterine routes or by the cytoplasm of the ovum, play a similar role in the genesis of mammary carcinoma of other species, including man. It is also evident that, at this time, these are mere postulations, although premature deductions are already appearing in the literature.

Although it is possible that the fundamental mechanism of transformation of normal cells to malignant neoplasms (the so-called intrinsic or formal genesis of cancer) is the same for all types of cells and all species of animals, the inciting factors leading up to the development of the malignant state (the so-called extrinsic or causal genesis of cancer) are obviously different for different types of neoplasia and different species of animals. In fact, it is just as possible that not all mammary carcinomas in one species of animal can be grouped etiologically. For example, it is not established that the mammary cancers of mice in which the milk agent is operative are the same as those induced by the administration of methyleholanthrene, or that the cancers of rabbits which develop on the basis of recurrent cystic disease are the same as those that arise as discrete adenomatous nodules in otherwise normal breasts.

Extrapolation from one species to another and from one type of tumor to another is not warranted at this incipient stage of knowledge of the nature of the neoplastic reaction. It is sounder, at least for the pragmatic purpose of encouraging further progress that must be derived from actual experimentation rather than theorization, to accentuate the careful, patient analysis of each possibly divergent type of cancer, with the well-founded hope that eventually this information may be synthesized into a coherent whole.

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## PARENTAL INFLUENCE ON MAMMARY TUMOR INCIDENCE

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THE degree of knowledge which we possess concerning the role of constitutional factors in the etiology of cancer of the breast differs markedly for mice and for human beings. This is not surprising, for it is mechanically much easier to observe the entire life span of mice not only for one but for many succeeding generations. It is also possible to isolate strains of mice by rigid and close inbreeding in a manner entirely impractical for human beings.

Anyone familiar with both types of material will recognize points of similarity and points of difference between them. He will, therefore, be extremely cautious in exchanging or in extending conclusions based upon data derived from either type of material alone. It will be well to examine some of the points of similarity which one finds in human beings and in mice in order to determine, if possible, the categories of experimental findings that might apply to both.

### SIMILARITIES IN THE MAMMARY SYSTEMS OF MICE AND HUMAN BEINGS

*Function.*—The function of the mammary system in both mice and human beings is the formation of milk for the feeding of the young from parturition until the development of the ability for independent ingestion of food.

*Cyclic Changes.*—The mammary system follows a series of cyclic changes which are closely related to hormonal activity.

*Hormonal Homology.*—As far as is known, the hormones controlling cyclic changes in the mammary system are the same in mice and in human beings.

*Sex-Limited Incidence.*—Largely because of different degrees of development of the mammary system in the two sexes, a situation which in turn may have a hormonal basis, the normal, functional male individuals rarely develop mammary cancer.

*Relative Age Distribution.*—In both mice and human beings the peak of mammary tumor incidence coincides with the period during which the reproductive activity of the female is on the wane. In both cases, also, the relatively few very early cases which occur tend to be more rapidly growing than those of the later age groups.

*Most Frequent Tumor Type.*—In both cases the most frequent type of malignant tumor of the mammary system originates in the adenomatous elements of the mammary tissue.

### POINTS OF DIFFERENCE

The points of difference are not listed in any particular order of real or apparent importance, but may be summarized as follows.

*Frequency of Metastasis.*—Metastasis of mammary tumors is much more frequent in human beings than in mice. This may be due in part, at least, to the



absolute size of lymph ducts and to the relative extent of tumor surface in the two forms.

*Amount of Dedifferentiation.*—Human mammary tumors tend to reach the "carcinoma simplex" degree of dedifferentiation more frequently than those of mice which retain more commonly recognizable adenomatous structure.

*Amount of Metaplasia.*—Mice more than human beings tend to show, in the tumor mass, areas of columnar squamous epithelial cells. Whether or not this is due to a more primitive type of tissue reaction in the mammary tissue of mice is uncertain.

*Relation to Lactation.*—Another possible point of difference is in the relative frequency of mammary cancer in virgin or in breeding females. In mice there is no instance on record in which the incidence of mammary tumors is higher in virgin animals than in breeding females of the same strain. Human data, however, seem to indicate different relationships. There seems to be a general and significant excess of cancer of the breast in unmarried women. Admittedly this classification is a social rather than a purely biologic one. The difference is difficult to explain although certain distinctions seem to hold good as follows.

(1) There will be a higher rate of pregnancy and of lactation among married women as a group than among unmarried.

(2) In so far as normal endocrine function is concerned there seems to be a greater chance that a higher proportion of normalcy will exist among married than among unmarried women.

(3) Abnormal endocrine unbalance is, in certain laboratory material, a predisposing factor in the formation of tumors.

(4) It seems reasonable that these facts may have some bearing on the situation, because the retention of female mice as virgins is carried out on a basis which does not recognize abnormal endocrine function nor are animals which are naturally abnormal retained in a stock because they are not successful breeders.

From this brief comparison it will be apparent that the points of similarity in the two types are much more basic in their biologic significance than are the points of difference. This fact should be borne in mind when clinical or experimental research on the etiology of human mammary tumors is being planned.

#### ETIOLOGY OF MAMMARY TUMORS IN MICE

We may next review briefly the experimental evidence on the various etiologic agents which affect mammary tumor incidence in mice.

A careful and thorough discussion of this problem has been developed by Bittner who distinguished three main avenues of influence as (1) genetic (chromosomal), (2) hormonal, and (3) through the milk. Each of these may be considered as being of importance in its own way. Apparently the most important is the last named. Its existence was demonstrated as follows.

When a "high tumor" strain is crossed with a "low tumor" strain the incidence of mammary tumors in the first hybrid generation animals depends

primarily upon whether the female parent comes from the high tumor or the low tumor strain. As an example of the tumor incidence in such a cross the following figures may be cited from Bittner.

High tumor ♀ × low tumor ♂ = mammary tumor incidence over 90 per cent.  
 Low tumor ♀ × high tumor ♂ = mammary tumor incidence under 5 per cent.

Inasmuch as the chromosomal complex in the two categories of first generation hybrid females was identical, it is evident that some powerful influence other than chromosomes is active.

The existence of this difference in the two types of hybrids was recorded by the staff of the Jackson Memorial Laboratory in 1933 and by Korteweg in Amsterdam almost simultaneously.

The next step was to locate, if possible, when and how the influence was transmitted from parent to offspring. This was definitely established by Bittner who fostered newborn young of the two types on nursing females of the opposite sort with the following results.

	NURSED BY ♀ FROM HIGH STOCK	NURSED BY ♀ FROM LOW STOCK
Hybrid ♀'s from high ♀ × low ♂	95.0% tumors	1.3% tumors
Hybrid ♀'s from low ♀ × high ♂	88.6% tumors	1.4% tumors

It is, therefore, clear that the process of nursing is able to transfer from the mother to the newborn young some influence that very largely determines the incidence of mammary tumors in later life.

Nursing as such is not the only way to transfer this type of influence, however. Bittner showed a significant increase in mammary tumor incidence when implants of bits of spleen from a high tumor strain were made in young animals of a low tumor type.

Woolley, Law, and Little also produced a similar result by inoculation of whole blood from high tumor strain animals into young, low tumor strain individuals.

All of these experimental procedures had to be carried out when the animals were young. The reason for this appears to be the fact that the degree of growth and type of mammary gland architecture differ in high and low tumor strains. Van Gulik and Korteweg showed a structural difference in the amount and extent of terminal bud formation in the branches of mammary glands and proved that "fostered" animals developed the general type of gland structure which characterized the strain from which the foster mother was selected.

Fekete, in a comparative study of the mammary glands of high and low tumor strains, has shown very interesting and important differences in behavior of the glands in the two types.

During pregnancy, twenty observations on mammary glands of low tumor females showed one structural or functional abnormality. This was acute mastitis in one female. During lactation sixteen observations showed three cases of acute mastitis and one case of obstruction of a nipple. During resting periods eleven observations showed one case of acute mastitis.

Similar periods observed in animals of a high tumor strain gave the following results. In pregnancy, twenty-one observations showed a large number of abnormalities as follows: Persistent growing area, one; thickened walls of ducts, two; chronic mastitis, two; acute mastitis and metaplasia, one; neoplasms, six; persistent secretory activity, two. In lactation, fifteen observations showed three cases of acute mastitis, two chronic mastitis, two neoplasms. During the resting periods, fifteen observations showed acute mastitis in three, areas of persistent secretion or growth in four, chronic mastitis and metaplasia in one, and neoplasms in two.

Persistence of secretion and growth, failure to adjust locally to the general physiologic level of the gland as a whole, characterized the animals of the high tumor strain.

These differences lead us to the second type of influence operative in the incidence of mammary tumors in mice, namely, those which are hormonal in nature.

It will be well to recognize that any classification based on such a term as "hormonal" will probably be broken down and redescribed as our knowledge of the causes of hormonal variation increases. It may be that the level of hormonal activity can be materially affected by some influence transmitted during nursing or during intrauterine development. It may be that chromosomal factors will be found which determine wide differences in degree of hormonal activity. In fact, one such gene affecting the activity of the hypophysis in mice has already been described and analyzed. It produces defective hypophyseal development and results in the animal being a sterile dwarf. There is every reason to believe that minor differences in degree of endocrine activity might also have a genetic basis.

While further data on the origin of hormonal differences are being collected, however, it is interesting to record the results of studies on the various inbred strains of mice that already exist. The incidence of mammary tumors is very clearly affected in at least one inbred strain of mice by the factor of pregnancy. This strain is the A albino strain, long inbred and, therefore, possessing a high degree of genetic uniformity. Breeding females of this strain produce about 88 per cent mammary tumors while those kept as virgins form only about 5 per cent. This condition may be contrasted with a high tumor stock such as C3H where both virgin and breeding females produce more than 90 per cent mammary tumors with no significant difference between the two groups. A condition intermediate between these two strains is found in the dba (dilute brown) stock where there seems to be about 80 per cent mammary tumor formation in the breeding females and 50 per cent in virgin females.

Endocrine influences on mammary tumor development were demonstrated beyond any doubt by the classic experiment of Murray who, by transplanting subcutaneously in castrated male mice of the dba strain an ovary from a sister animal, caused a considerable number of these "feminized" males to develop mammary tumors. These neoplasms were of the same general type as those commonly developed by virgin females of this same strain of mice.

Lacassagne later showed that it was the estrogenic hormone of the ovary that produced the conditions necessary for mammary tumor development in male animals.

Evidence that absence of ovarian hormones decreased the likelihood of mammary tumor formation in mice of this strain has also been recorded by Murray. Whether, and if so to what degree, this relationship exists in human beings is debatable.

A third type of influence is that exerted through orthodox genetic channels, namely, the chromosomes.

Evidence for this influence is somewhat difficult to obtain because the strong effect of the milk influence and the complications which are introduced by variation in hormonal activity tend to mask the less powerful genetic effect. Bittner, however, has clearly shown that the genetic influence exists and that it is more evident in  $F_1$  generation hybrids than in those of  $F_2$  and subsequent hybrid generations. The quantitative relationship between  $F_1$  and  $F_2$  hybrids and between  $F_1$  hybrids and a backcross between such animals and a low tumor strain suggests that the situation may be eventually analyzed.

The relative incidence of mammary tumors in the three generations of a cross reported by him is as follows:  $F_1$ , 95 per cent;  $F_2$ , 76 per cent; backcross, 53.5 per cent.

If the genetic influence was due to a single Mendelian dominant, the expectation in this material would be:  $F_1$ , 100 per cent;  $F_2$ , 75 per cent; backcross, 50.0 per cent.

Very clearly the observed results, in so far as they go, are consistent with that interpretation. They should not, however, be considered as conclusive of the point at issue.

#### HUMAN DATA

The absence of anything resembling a strain of inbred human beings with known mammary tumor incidence at once limits the study to statistical methods. It would, however, be of the greatest importance to conduct such studies and they would not be unduly difficult or complex. Incidence of all types of neoplasms in a sufficiently large population of surgically ovariectomized women would be of distinct value in comparison with that in a similar sized population of the same age and degree of reproductive activity, with no operations. It might well reveal some results that would provide a basis for estimating more exactly the degree of correspondence or difference between the human and the laboratory material.

Similarly, if one reviews the literature on the genetics of cancer in human beings he is struck with two important facts, or, perhaps better, attitudes on the part of investigators. The first of these is the reliance on human pedigree data which is one of the commoner ways of presenting evidence of hereditary tendencies. It will take only a moment's consideration to realize that unless the individuals included in these pedigrees have been directly observed, the evidence which they present is secondary in nature and must involve at least

some of the factor of heresay. No amount of careful analysis of primary data, which in fact are not completely accurate, can provide the degree of accuracy which is lacking.

Since no institution has collected direct observational records on several generations of human beings one cannot use the published data as confirmation or denial of the application of principles which have been demonstrated in laboratory animals.

This does not mean that the imperfect data on human beings are without value. Such data can be and are *suggestive*. In so far as they go they indicate the probability of familial tendencies to develop not only cancer in general, but cancer of the breast in particular.

The second "attitude" is that seen in extensive and comprehensive statistical studies. Here again the presence of cancer and the subsequent classification of the individual as "cancerous" depend upon the cause of death as recorded by many observers. These observers have different degrees of training and of scientific responsibility and reliability. There is no way of determining the relative degree of accuracy of their records. For this reason massed statistical data must also be evaluated as being of limited importance. They also can be suggestive but not conclusive.

The problem of parental influence in the formation of mammary cancer in man is one which can and should be investigated. Its study would involve direct observation and a program of sufficient duration to enable the research worker to contact two generations at least.

It should be possible to obtain records of several hundred or perhaps 1,000 women who have proved adenocarcinomas of the breast and who have had three or four children now adults. By dividing the progeny according to whether or not they were nursed or were only bottle fed, two groups can be set up. If cancer of the breast in human beings follows the same general type of behavior as mammary cancer in mice, the daughters of cancerous women, especially those nursed by their mothers, should show definitely more cancer of the breast than of organs other than the reproductive system. They should also show more cancer of the breast than their brothers show cancer of any one type. These facts, if established, would do a great deal toward indicating the next line of research to be undertaken.

The demonstration of the existence of a "milk influence" in human beings would at once open the way for a new series of experiments on hormones and on the chemical analysis of the milk itself. It should be relatively easy to dispose of this question in one way or the other even before any specialized center for the study of human biology has been established.

#### SUMMARY

1. The experimental evidence derived from a study of the etiologic factors affecting mammary tumor incidence in mice indicates that there are three main groups of influences:

(a) "Milk" influence transferred during the period of nursing.

(b) Hormonal influences possibly having a genetic basis.

(c) Chromosomal influences possibly affecting the structure and/or the reaction of the mammary tissue and also the rate and amount of endocrine activity.

2. The results are sufficiently important to justify a study of human material to discover to what extent the conclusions based on laboratory animals may properly be extended to human beings.

3. Care should be exercised in recognizing the limitations of present methods of collecting and analyzing human data.

4. With reasonable foresight and moderate resources much could be accomplished over a five- to ten-year period.

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# THE PROGNOSIS OF BENIGN LESIONS OF THE FEMALE BREAST

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WHILE a large and as yet undetermined number of cancers of the breast appear to arise without antecedent pathologic change, certain benign lesions predispose to the development of mammary malignant tumors. Some of these lesions have been almost universally regarded as precancerous; some controversy has existed as to the significance of others. At least a portion of this uncertainty was based on confusion in terminology of the lesions.

The more important lesions of the breast will be defined for the purpose of clarity, and their relation to cancer considered.

Many lesions of the breast are variable in extent and degree. Moreover, a breast may not present uniform characteristics throughout, and its physiologic lability further complicates the picture. In any attempt to classify such lesions these points must be kept in mind.

## HYPERTROPHY

At or following puberty, one or both breasts may enlarge to an excessive degree. The enlargement does not produce symptoms other than those referable to its size. The consistency is essentially that of a normal breast. On section the breast tissue is diffusely fibrotic. When studied microscopically the enlargement is found to be due chiefly to increase in the connective tissue elements, sometimes associated with periductal edema. The fat may also be considerably increased, but enlargement in breasts which show an appreciable amount of fat should be considered as due probably to obesity rather than to hypertrophy. The epithelial elements of the breast take little part in the process, although there is some increase in the ductal elements. Assays of the urine of these patients for estrogenic hormones usually show the estrogens to be within normal limits, although they may be slightly elevated.<sup>1</sup> This condition does not predispose to the development of carcinoma.

## ADENOFIBROSIS

The breast in the lesion of adenofibrosis is diffusely fibrotic or finely nodular. In the early stages the breast shows cyclic swelling, more marked premenstrually and lessening with menstruation. Later, the slight to moderate increase in size becomes permanent. Pain, which is the feature of the process that usually brings the patient to the physician, is ordinarily more severe in the premenstrual period and is relieved by menstruation. The swelling and pain may be accompanied by venous engorgement. The parenchyma of the breast is somewhat

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rubbery. In the earlier stages, the increased consistency may be somewhat focal or even give a finely nodular texture but later the regions of firmness tend to coalesce, producing a single solid mass with rather clearly defined edges. On section the breast shows a fairly uniform dull white color and is clearly fibrous in nature. Through the firm, white, somewhat resilient connective tissue will be scattered small gray or gray-pink foci. Microscopic study reveals these to be regions of periductal and periacinar edema, often with lymphocytic infiltration. Later the collagen is fairly dense. Changes in the epithelial elements are not significant and do not constitute an integral part of the process. Study of hormonal output has not revealed definite abnormalities.<sup>2</sup> This condition rarely persists beyond the menopause; it is not known to be precancerous.

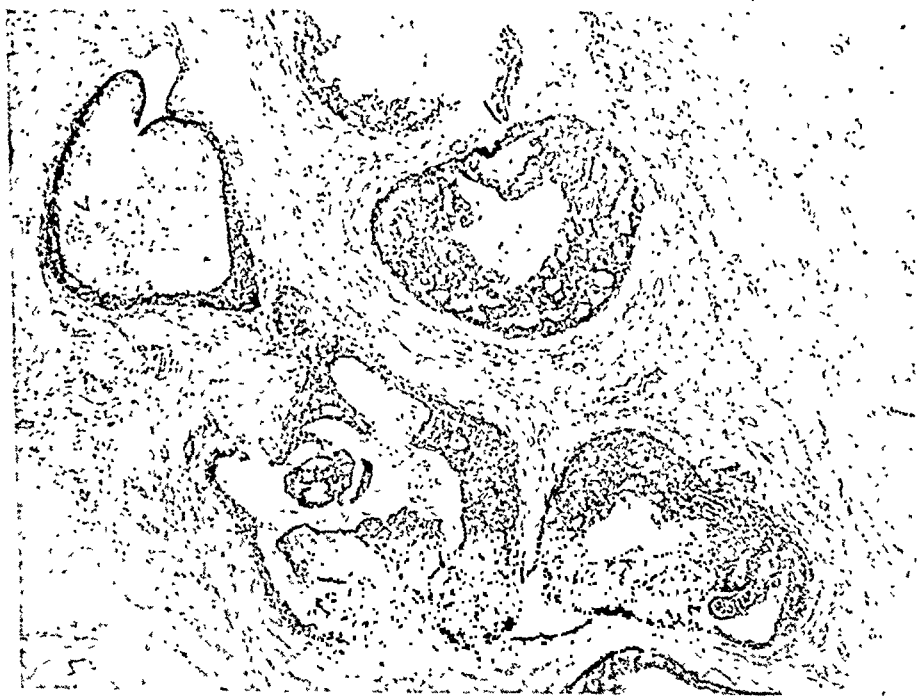


Fig. 1.—Focus of chronic mastitis showing slight epithelial hyperplasia.

#### CHRONIC MASTITIS

The lesion of chronic mastitis is probably basically adenofibrosis with epithelial proliferation of a mild type or abnormal secretory activity of the mammary epithelium superposed. There may be serous discharge from the nipple. Certain of the cases classified by Nathanson<sup>1</sup> as "nonpuerperal secretion" and by Semb<sup>3</sup> as "microcystic fibroadenomatosis" belong in this group. On palpation of a breast of this type, somewhat granular or nodular and at times firm cordlike structures may be felt, often radiating out from the region of the nipple. The nodules are not hard but somewhat elastic. On section the breast tissue is dull white or sometimes shows a faintly brownish tinge and a scattering of small cystic spaces not much more than visible to the naked eye. Inspissated secretion in small amounts may sometimes be squeezed from the sur-



face. This lesion has been described by Cole and Rossiter as "benign parenchymatous hyperplasia."<sup>4</sup>

Microscopically periacinar and periductal connective tissue is increased and is often edematous. Lymphocytic infiltration may occur. This was the justification originally for calling this lesion "mastitis" but the infiltration is probably not inflammatory. Some dilatation of the ducts will be apparent, the lumens often containing secretion and epithelial debris. Ordinarily the epithelium of the ducts and acini is slightly hyperplastic. In extreme cases the proliferated epithelium may practically fill the ducts. At times there may be in the breast foci of closely packed, almost solid masses of ductal and acinal

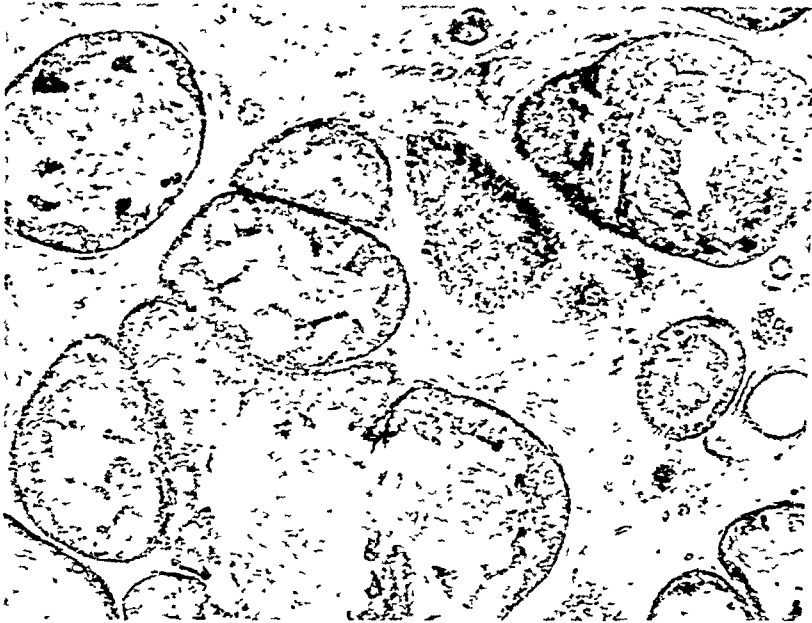


Fig 2.—Chronic mastitis with marked epithelial hyperplasia and retained secretion.

epithelium, which superficially resemble neoplasia. As was wisely pointed out by Bloodgood,<sup>5</sup> these foci are actually benign in spite of the somewhat bizarre and highly cellular picture that they may present. In its more marked forms, this condition, unlike adenofibrosis, may persist after the menopause. The lesion is probably due to endocrine dysfunction in which the normal cyclic character of the secretion of estrogens has been disturbed. As Nathanson<sup>1</sup> pointed out, the process might be caused by continuous estrogenic stimulation lacking the counterbalance of adequate production of corpus luteum hormone. Somewhat similar changes may be produced in mice by repeated injection of estrogens.<sup>6</sup>

In its milder forms this lesion is not precancerous but in those in which marked epithelial hyperplasia occurs, it must be considered as precancerous. Of special interest in this regard is the use of excessive amounts of estrogenic hormone in women for various purposes. There are instances in which the prolonged use of large doses of estrogens has apparently stimulated proliferation of mammary epithelium with the ultimate development of carcinoma, although such

occurrence has not been proved beyond question. Of interest are the experiments of Lacassagne.<sup>7</sup> Male mice practically never showed breast carcinoma, even in strains of mice selectively bred for a high incidence of mammary carcinoma in females. The prolonged administration of estrogenic hormones to the males produced considerable development of mammary tissue, and in this hyperplastic breast tissue developed a proportion of mammary carcinomas comparable to that in the females.

#### CHRONIC CYSTIC MASTITIS

Chronic cystic mastitis presents a variety of forms. The one common factor is the development of cysts readily visible, single or multiple. As has been pointed out by a number of observers, these cysts may have entirely lost their epithelial lining, they may be lined with essentially normal epithelium, or they may be lined with epithelium showing varying degrees of hyperplasia and intracystic papillary proliferation. The blue-domed cyst described by Bloodgood usually does not show epithelial hyperplasia in its lining and is then in itself harmless. However, it may be only one feature of a chronic cystic mastitis in which there may be a considerable amount of epithelial activity. When a solitary cyst occurs, this usually is the result of occlusion of a portion of a single duct. Chronic cystic mastitis is most common toward the end of the childbearing period or just after the menopause. As Nathanson<sup>1</sup> pointed out, conditions such as adenofibrosis or chronic mastitis may precede the development of chronic cystic mastitis. Pain is usually absent. Cyclic swelling is not an integral part of the process. A lumpiness of the breast, either localized or generalized, is the chief clinically distinguishing feature. It cannot be too clearly emphasized that given an isolated nodule in the breast, it is impossible to distinguish by physical examination between localized cystic disease and early carcinoma. The nature of such a lesion should be determined by biopsy. After removal of a breast with chronic cystic mastitis, section may show one or more thin-walled bluish cysts varying from several centimeters to a few millimeters in diameter in some portions of the breast tissue and, sometimes elsewhere, masses of inspissated material in dilated ducts or acini or, still elsewhere, grayish, opaque pultaceous or granular circumscribed foci from which, on pressure, a gray or yellowish material may be expressed. The presence of a typical blue-domed cyst is no guarantee that the remainder of the breast tissue is normal and free from malignancy. More than once it has been my experience in sectioning a breast to find present a carcinoma that had not been palpated by the surgeon entirely aside from the cyst which had led to the operation.

Nathanson<sup>1</sup> found no consistent pattern of excretion of estrogens in patients with cystic disease. However, the administration of estrogens with or without prolactin will lead to the production of cystic disease in the experimental animal.

As has already been said, on microscopic observation there may be found a single flattened layer of epithelium lining the cyst or this may have atrophied and left present fibrous tissue alone. There is every gradation from this atrophic lining through several layers of polyhedral epithelial cells to the active proliferation filling the duct with evidence of cellular anaplasia and mitotic activity, which lacks

only the occurrence of stromal invasion to warrant the diagnosis of carcinoma. As Cheatle and Cutler<sup>5</sup> pointed out, "the carcinoma process in the breast begins in an epithelial neoplasia in ducts and acini which continues to grow there before and after there has been a transgression of normal boundaries. . . ." Since by external examination there is no sure way of distinguishing between those forms of chronic cystic mastitis which show little or no epithelial activity and those



Fig. 3.—Chronic cystic mastitis with intraductal hyperplasia precancerous

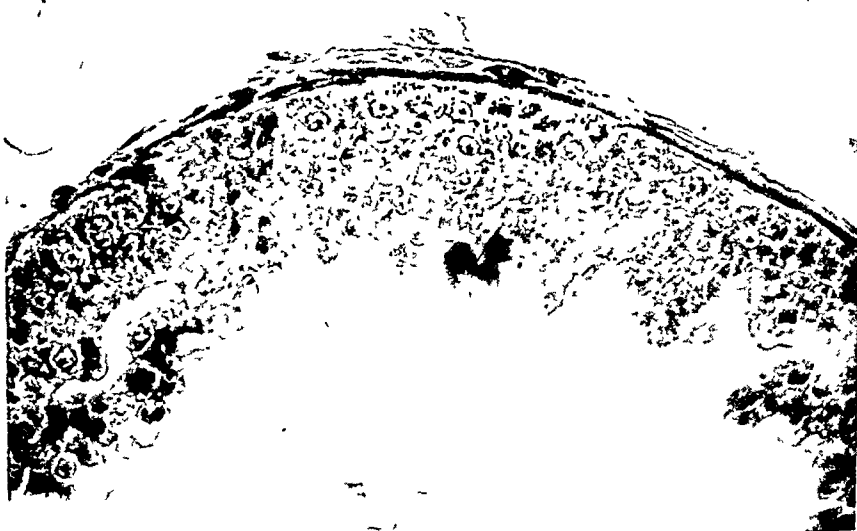


Fig. 4.—Hyperplastic epithelium in chronic cystic mastitis

which show marked epithelial hyperplasia, the disease must be considered as precancerous.

The follow-up studies carried on in this laboratory several years ago<sup>9</sup> were based on those women who had developed chronic cystic mastitis and the remainder of whose breast tissue had been allowed to remain in place after excision of the local lesion in the breast. Since the worst foci of mastitis were removed, and apparently normal breast tissue left behind, these women should have been partially protected from the development of cancer. However, it was found that in the age group from 30 to 49 years, patients with chronic mastitis and chronic cystic mastitis showed 11.7 times as much carcinoma of the breast as the Massachusetts female population of comparable age. In the women over 50 years of age, 2.5 times as much breast cancer developed. Averaging the entire group, 4.5 times as much breast carcinoma occurred in the group with chronic mastitis and chronic cystic mastitis as in the normal population. On the basis of this and other studies, we can therefore establish the following general rule for the management of chronic cystic mastitis, which must be considered as a precancerous lesion.

If chronic cystic mastitis be localized and the woman be under 50 years of age or be particularly desirous of keeping the breast, no further therapy beyond the removal of the palpable mass is immediately indicated. Such a patient should be followed at semiannual intervals and if a further mass develops, either a simple mastectomy or a radical mastectomy should be done according as the mass is determined to be benign or malignant. Since the lesions in both chronic mastitis and chronic cystic mastitis are apt to be bilateral, the logical procedure would be to amputate both breasts. There is not sufficient risk of subsequent development of carcinoma, however, to warrant or justify bilateral mastectomy. In this opinion Geschickter concurred.<sup>10</sup>

If, on excision of a focus of chronic cystic mastitis or chronic mastitis, there is found evidence of definite precancerous hyperplasia, a simple mastectomy should be performed on the affected side. As has been emphasized by Cole and Rossiter,<sup>4</sup> it is incumbent on the pathologist to take an adequate number of blocks of breast tissue chosen from grossly suspicious areas to determine whether or not the precancerous hyperplasia exists.

#### INTRADUCTAL PAPILLOMA

Intraductal papilloma of the breast is essentially a complex papillary mass projecting into the distended lumen of a duct. The papillary mass is made up of complexly branching stromal bands often arranged in a frondlike pattern and usually attached at only one point to the wall of the duct. These stromal bands are coated over with epithelium similar to that lining the duct. The epithelium is usually cuboidal, rarely columnar. The most common site is within 2 cm. below the areola although they may be found elsewhere along the course of the ducts. The attachment of the intraductal papilloma is usually by a single stalk, although there may be several. Since the stroma is quite vascular, oozing may occur from its blood vessels, and either bloodstained or frankly bloody discharge from the nipple may result.

## THE BLEEDING NIPPLE

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THE small number of articles in the American literature of the past ten years dealing with bloody discharge from the nipple would suggest a general acceptance of the significance of this symptom and no challenge to the therapeutic measures recommended.

Variously advocated are simple excision, segmental resection, simple and radical amputation, thus allowing very considerable latitude in procedure adopted for those cases in which frank cancer is not demonstrable.

A brief review of the subject and an outline of procedure is offered in the hope that, without sacrifice to the patients' security, more limited operations and fewer simple amputations will become the practice.

### REVIEW OF LITERATURE

The significance of a discharge from the nipple, particularly a bloody discharge, has been variously interpreted. Adair, Judd, and Miller and Lewis have found about the same proportion of benign and malignant lesions responsible for this symptom. MacNeal and Cheate regarded bleeding as of grave significance.

On the other hand, Cutler and Floyd and Haggard thought that in the majority of cases bleeding was due to small benign duct papillomas and rarely to malignancy. Hart, considering only papillary cystadenoma, found that 48 per cent of the benign, and 12 per cent of the malignant, cases showed discharge as the most prominent symptom. Joel has never seen malignant degeneration in his cases of bleeding breasts. For twenty-three years, Knoflach and Urban did follow-up studies on thirty patients operated upon for bleeding nipple and ten not operated upon. In none did carcinoma develop. According to Bloodgood and Peek and White bleeding is only a symptom and, occurring without palpable tumor, does not demand treatment. Hellwig, Hart, and Floyd and Haggard contented themselves with local excision unless malignancy was found. Hinchey found cancer as the cause of discharge of all kinds, sanguineous and nonsanguineous, in 36 per cent of his cases. Stowers found malignancy in four of ten patients having bloody discharge from the nipple.

Undoubtedly the difficulty in distinguishing between actively proliferating adenoecystic disease and cancer has complicated the problem of determining the true incidence of malignancy in patients with bloody discharge.

Bloodgood has aptly called these "borderline tumors" and has pointed out the extreme rarity in which axillary metastases are found. To the unknown degree that pathologists have diagnosed these borderline lesions as cancer, the percentage of malignancy associated with bleeding has been exaggerated.

## FREQUENCY

Sanguineous discharge from the nipple is not a common symptom. Reported series of cases are small. Hinchey quoted Geschichter that, of 5,118 patients coming to Johns Hopkins Hospital because of a breast complaint 6 per cent had bloody discharge.

In 1934, I reported 233 cases of cystic disease, among which there were 8 patients who had bleeding. Of 543 cancers of the breast upon which a radical amputation was performed at the University Hospital, 18 had bloody discharge.

The 55 cases reported in this article represent the total number of patients admitted to the 450 bed Minnesota General Hospital and to a 150 bed private Minneapolis hospital.

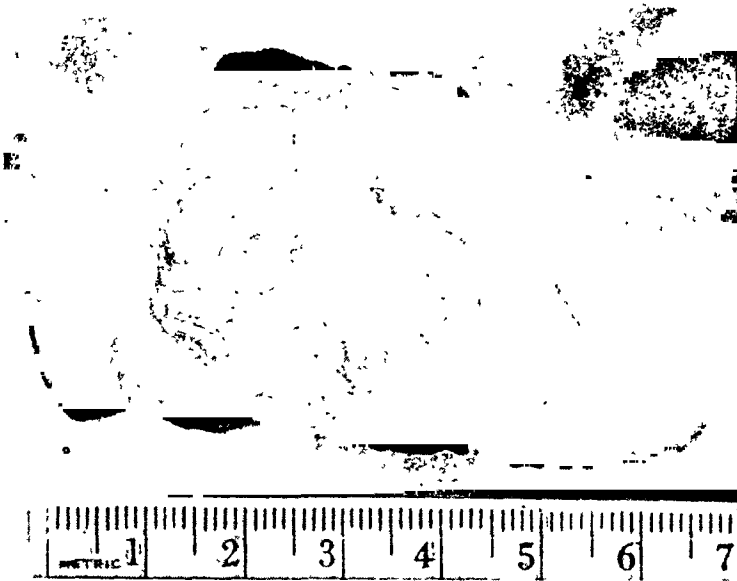


Fig. 1.—A large solitary intraductal papilloma; note the dilated duct and the papilloma lying free except for the base. The papilloma will be centered in the base and in whether or not there is any surrounding stroma.

## ETIOLOGY

The experience of a number of investigators has shown that duct papilloma, carcinoma, and cystic disease are responsible for most of the cases of bloody discharge from the nipple. In the series here reported there were nineteen patients with duct papillomas, twenty-one with carcinomas, thirteen with cystic disease and one with dilated ducts only. In one additional case, exploration was not done, but because discharge has ceased and the case has been followed for nine years, it is assumed that the lesion was benign. The benign lesions totaled thirty-four and malignant lesions twenty-one, approximately 60 per cent benign and 40 per cent malignant.

Other etiologic factors not encountered in this series but reported in the literature are (1) inflammatory lesions, (2) traumatic lesions, (3) hormonal dysfunction, (4) sarcoma, and (5) Paget's disease. Because bleeding is a symptom and not a diagnosis, and because the record rooms did not have a separate

listing for discharge, it is quite likely that a few cases in which surgery was not done have been missed.

#### DIAGNOSIS

The character of the discharge is merely suggestive. As this discussion is limited to bloody discharge, and since bloody discharge is rightly regarded as of *more serious significance than other types*, it is well to remember that all types of discharge (with the exception of galactorrhea) need investigation. The outline of procedure which follows may well be applied to patients with non-sanguineous discharge.

Diagnosis is essentially a problem for the pathologist. Frozen sections are not to be relied upon. Because cancers associated with bleeding from the nipple are usually of low malignancy and also because the differentiation between



Fig. 2.—Several ducts are filled to varying degrees by papillomas—a good example of diffuse papillomatosis. This lesion commonly occupies a number of ducts and when it is sufficiently disseminated in the breast simple amputation may be required.

cancer and adenocystic disease may be difficult, the surgeon should permit the pathologist time to prepare and study permanent slides.

In the absence of palpable tumor there are three diagnostic aids for the localization of the source of bleeding:

1. Transillumination, as described by Cutler, is easily applied and often definitive if sufficient blood is present to outline a duct, papilloma, or papillomatous cyst.

2. Mammography has been enthusiastically recommended by Hicken and his co-workers. Attempts using this method have been deterred because of severe tissue reactions as reported by Romano and McFetridge and by Sowers and Masson.

3. Pressure tests have proved most useful in our hands. Point pressure by the finger on the various segments of the areola will usually indicate which

TABLE I. SOURCE OF DISCHARGE

Single polyps (14)	
Diffuse papillomas (5)	19
Cystic disease	13
Dilated ducts	1
Undetermined (not operated)	1
Total benign lesions	34
Cancer	21
Total patients with bloody discharge	55

duct contains the blood. Often the affected duct, or ducts, stands out a little more distinctly than its neighbors.

## TREATMENT

Of the thirty-three nonmalignant lesions twenty-three, or 69.6 per cent. received either local excision or segmental resections, thus permitting the breast to be saved. Of the ten simple amputations, three were done for diffuse papillomata of ducts, two for single papillomas, and five for adenocystic disease sufficiently diffuse to warrant total removal of the breast.

## SUGGESTED PROCEDURE

Accepting the dogma that it is better that a woman lose her breast than her life, the determination of the extent of the procedure to be done in any given case is still not easy. To most women the loss of a breast is a tragedy and a definite psychic shock. No one has been able to determine the number of breasts which justifiably may be sacrificed to save a life.

The following outline in general has been the practice and teaching of the department of surgery at the University of Minnesota and bears the approval of the department of pathology.

*A. Discharge and Palpable Tumor.*—The presence of the tumor alone is sufficient justification for its removal. Local excision may suffice for solitary intraductal papillomas and well-localized adenocystic disease but because the sources of bleeding may be multiple it is better practice to excise the entire duct and its tributary glands. The technique described by Babcock has served well in accomplishing such a limited resection. Only when the pathologist has satisfied himself that the lesion is malignant is radical amputation justified.

*B. Discharge and Diffuse Nodularity.*—A segmental resection of the duct containing the bloody discharge and its tributary system is done. If cancer is not found and the source of bleeding is eliminated the attitude toward the remaining breast will depend upon the surgeon's attitude toward the role of cystic disease as a potentially precancerous lesion. If he holds the prevalent opinion that the relationship is not close, he will content himself with keeping the patient under observation, always ready to explore any localized area which shows increase in consistency or stands apart from the rest of the breast.

TABLE II. OPERATIVE PROCEDURES

Local excisions or segmental resections (breast preserved)	23
Simple amputations	
Single polyps	2
Diffuse papillomas	3
Diffuse cystic disease	5
Total operations on benign lesions	33



*C. Discharge and No Palpable Tumor or Demonstrable Breast Change.*—

Whenever the source of bleeding can be located the offending duct and tributary glands are excised. Where the discharge is intermittent or scanty it may be difficult to locate the segment of breast or the duct from which the discharge is coming. Under these circumstances it seems entirely reasonable to keep the patient under observation. Repeated examinations will usually permit localization.



Fig. 3.—An example of a mild form of adenocystic disease which is causing bloody discharge; nothing is seen in microscopic study to indicate why the lesion produces bleeding.

The justification for this policy is based upon the extreme rarity of sanguineous discharge from the nipple caused by cancer and without palpable tumor. Bell stated that in his entire experience as head of the department of pathology at the University of Minnesota there have been no examples of such an occurrence. It is entirely possible among patients showing bloody discharge that an early, small, deeply developing cancer can exist without palpable tumor. Hinchey reported two cases, and Koucky, pathologist to several private hospitals in Minneapolis, has experienced it but once in over 5,000 breast biopsies.

*D. Bloody Discharge From Multiple Sources.*—A waiting policy is here indicated unless palpation reveals changes in breast consistency which then justifies biopsy of the most suspicious area. Bleeding of such nature may subside spontaneously. I have observed such a case, occurring bilaterally at the end of a period of lactation and subsiding completely within a few months. Papillomas may undergo fibrotic changes, even calcification.

*E. Pseudosanguineous Discharge.*—A dark green, sometimes grumous discharge from the nipple may easily be mistaken for bloody discharge. When a single duct is the source, excision is warranted for the patient's peace of mind. The excised duct will show ectasia only. There will be little or no sign of

epithelial activity. The dilatation may involve even the smaller tributary ducts in the periphery of the breast. When multiple ducts are involved and no masses except the ducts themselves are palpable, the condition need not be disturbed since sacrifice of the whole breast is unnecessary.

*F. Persistent or Nonlocalized Bleeding.*—Persistent bleeding from multiple sources or bleeding which cannot be localized may warrant simple amputation. Especially is this true in older women where the loss of the breast is not a tragedy, or where the patient herself may elect to end her state of uncertainty or apprehension. It is difficult to be dogmatic in advising a patient to accept amputation because percentagewise, even with the symptoms listed, she may still carry her greatest total risk from cancer arising in other sites than the breast. If she elects to keep her breast, who can say that she is not justified?



Fig. 4.—Adenocystic disease with marked intraductal epithelial growth; note blood filling the duct spaces. Some pathologists call this carcinoma grade I. Others believe it is benign, but all will insist that the entire lesion be removed from the breast.

#### SUMMARY AND DISCUSSION

It is my conviction that too much fear, even panic, has been exhibited toward the symptom of bloody discharge from the nipple. It is my conviction that a truly representative report of all cases would reveal a lower percentage of malignancies responsible for the symptom. The inadequacies of the filing systems which do not provide for indexing the symptom of bloody discharge undoubtedly account for the loss of some benign cases from this series, whereas all of the cancers are included. Then, too, it is likely that procrastination or subsidence of symptoms deters a certain number of women from reporting the bleeding, whereas all malignancies eventually drive the patient to seek medical attention.

Bloody discharge can never be overlooked or ignored until cancer has been ruled out. In younger women where the source of the bleeding cannot be localized, where it is intermittent, recurrent, or involves a number of different ducts.

and no palpable tumor exists, the patient's hazard does not merit removal of the breast. Likewise, in younger women when the source of bleeding is revealed to be adenocystic disease, even though the remainder of the breast may harbor more of the disease, it is my opinion that local excision is sufficient. Unless further bleeding develops which requires investigation, the patient should merely be kept under observation as any other patient who manifests adenocystic disease.

Whether the surgeon believes that there is no relationship between cystic disease and cancer, or whether he believes that the incidence of cancer is higher in adenocystic disease, the risk does not justify the removal of breasts in young women. In later life when the period of function is past and the loss of the breast is less of a tragedy the situation may be altered. If the surgeon believes that the patient is exposed to a greater than ordinary risk of cancer because of the breast condition and the patient agrees that she does not wish to undergo the risk, a simple amputation may be done.

In seeking to preserve breasts by the application of these views, I know of no instance where this advice or plan of procedure has resulted in delay or failure to recognize a malignancy.

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# INTRADUCTAL BIOPSY OF CERTAIN PATHOLOGIC PROCESSES OF THE BREAST

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AS A complement to the roentgen-ray study of the duct system of the breast, and in cases of evident lesions of the milk duct or its main branches seen on the x-ray film, a curettage or biopsy of these processes has been performed endo-ductally. Thus, this has presented one more opportunity for the diagnosis and treatment of mammary diseases.

Intraductal growths that frequently are found near the nipple, and which dilate the ducts as they develop, are the lesions most suitable for this new diagnostic procedure.

In previous articles I have pointed out that when injecting a milk duct, especially if there is a reflux of the liquid, abundant ductal secretions are emitted, and also small tumoral fragments in cases of intraductal growths, which afford a proper histologic examination.

## TECHNIQUE

The technique of the intraductal biopsy consists of two steps: first, radiographic localization of the pathologic process, that is, determination of the diseased tubular-acinous gland and localization of the pathologic process in it, and, second, the biopsy. The first part is a purely x-ray technical problem, and it shall only be stated here that as contrast media we employ concentrated iodized solutions used in intravenous urography.

Once the pathologic process which we desire to curette is localized, the biopsy is then done by two stages. First, the slow dilatation of the orifice of the milk duct is accomplished by means of small metal dilators, such as are used in ophthalmology for the dilatation of the lacrimal orifice. Lubrication of the nipple with olive oil facilitates these operations.

In certain cases the dilatation is completed with the use of a small bougie (Laminaria), which must be introduced slightly in order to dilate only the sphincter of the ductal orifice. Care must be taken that it is not introduced too far, as some difficulty may be found in extracting it. In such circumstances a slight local anesthesia proves useful.

Second, after securing sufficient dilatation to permit the introduction of one of our delicate instruments, with a fine curette, wire loop, or small forceps (according to the type of lesion and size of the duct), the biopsy is easily obtained. The pathologist is able to make a satisfactory histologic study from the specimens obtained in this manner.

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Thus, the problem of bleeding from the nipple is partially solved; the x-rays will show whether or not there exists an intraductal neoplastic growth, and they will give us information as to its extension, location, number, and probable etiology, which will often be confirmed by the histologic study of the biopsy obtained endoductally.

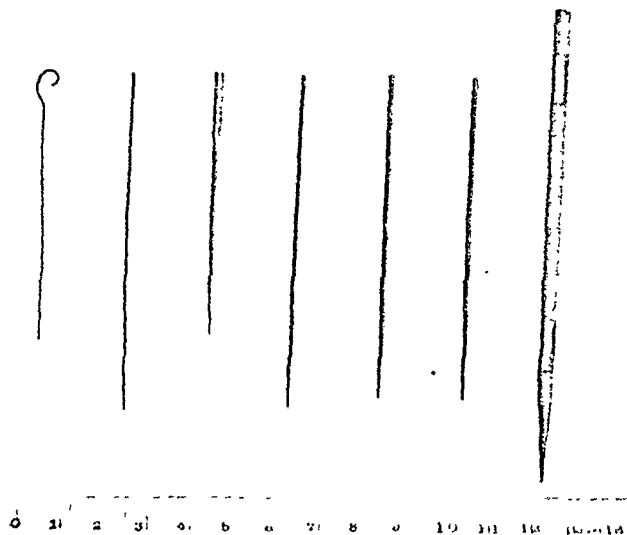


Fig. 1.—Dilators of the milk duct orifice.

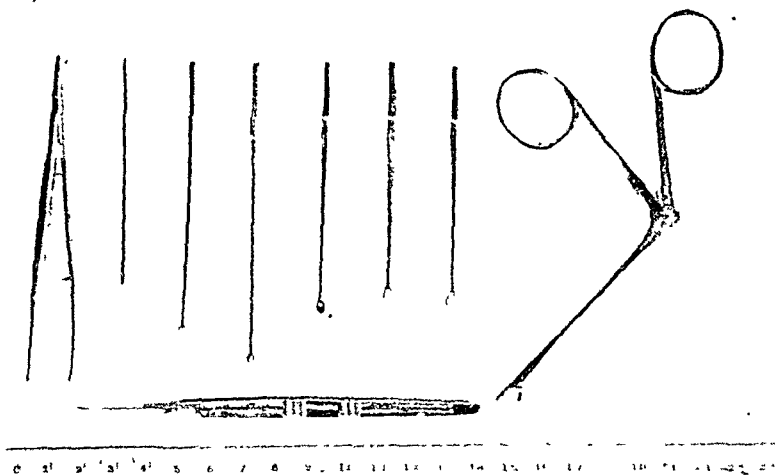


Fig. 2.—Different instruments used for biopsy.

When the biopsy reveals only a benign papillary lesion the possibility must never be absolutely discarded of a malignant transformation in that part of the tumor from which no biopsy was taken, because these lesions must be looked upon as precancerous conditions, and this transformation must always be suspected in large papillary adenomas, notwithstanding a negative biopsy.



Fig. 3.

Fig. 3.—Intraductal growth, obstructing a milk duct, in a 17-year-old patient with bleeding from the nipple, no lump was present.

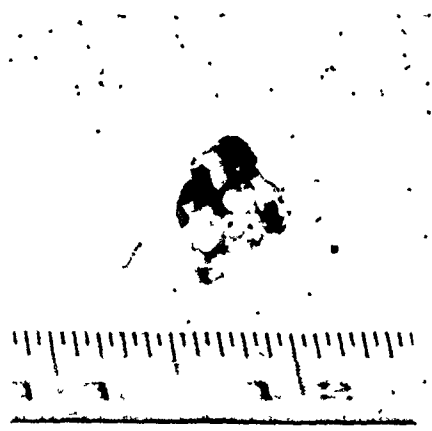


Fig. 5.

Fig. 5.—Photograph of the biopsy specimen taken from the same patient as that of Fig. 4.



Fig. 4.—Three stages in the dilatation of a ductal orifice and insertion of the wire loop for the biopsy, continuation of the preceding case.

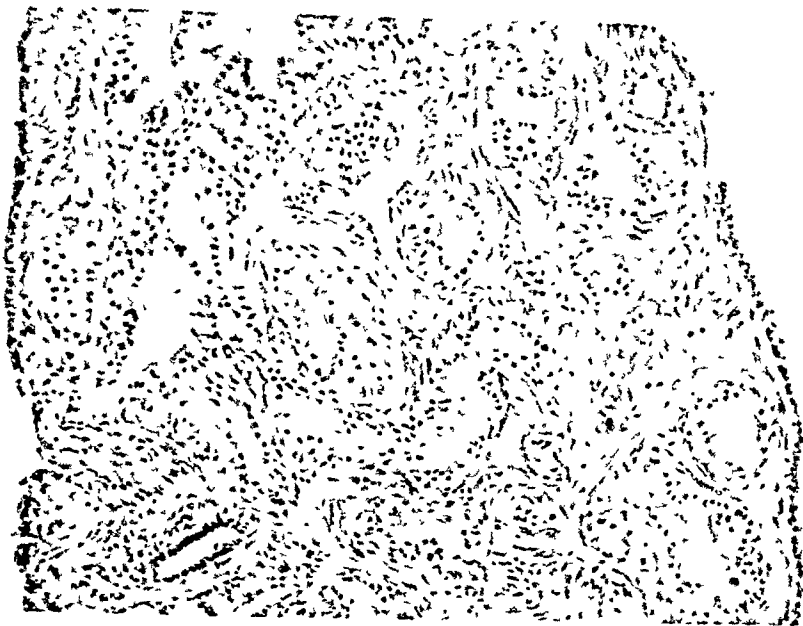


Fig. 6.—Microphotograph of the same specimen as shown in Fig. 5; intraductal fibroadenoma with malignant transformation. (Histologic study by Dr. Pou de Santiago.)



Fig 7.



Fig 8.

Fig. 7.—Partial mastectomy performed by Professor H. May, on patient of Figs. 3 to 6. The pathologic study by Professor Carlos M. Dominguez proved the existence of a malignant intraductal tumor.

Fig. 8.—Sixteen-year-old patient with a five-day bleeding from the nipple; no tumor was present. The x-ray shows a dilated milk duct and multiple annular images that correspond to the opaque substances disposed around the endocystic growth-image of papillary carcinoma. An intraductal biopsy was taken



Fig. 9.—Microphotograph of the biopsy specimen from the patient shown in Fig. 8; intraductal fibroadenoma with malignant transformation. (Histologic study by Professor Carlos M. Dominguez.)

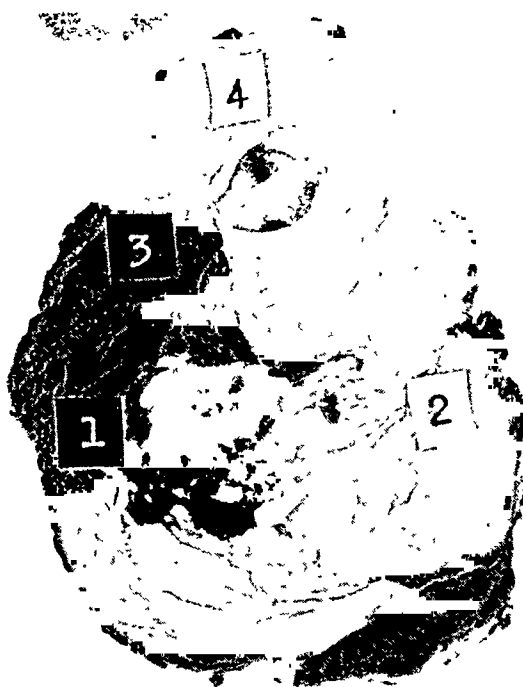


Fig. 10.—Mastectomy performed by Professor Julio Nin Y Silva on patient of Figs. 8 and 9. Pathologic study by Professor Carlos M. Dominguez: (1) Intracystic papillary fibro-ignant transformation; (2) smaller tributary ducts of the larger cystic their source by the tumor; (3) milk duct that continues at (4), section milk duct unfolded at the base of the nipple.



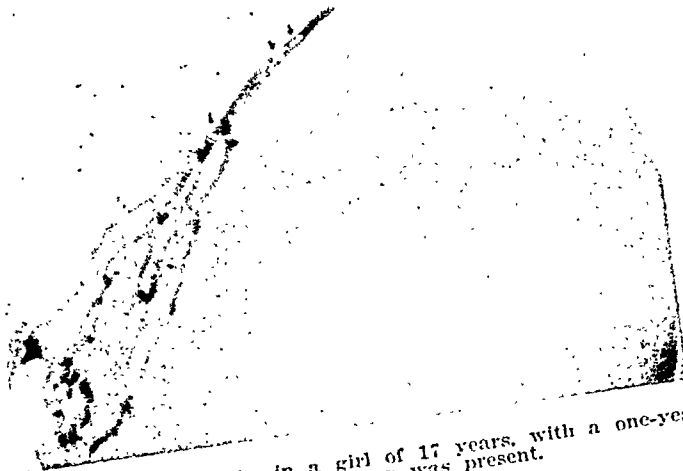


Fig. 11.—Various intraductal growths in a girl of 17 years, with a one-year bleeding from the nipple; no lump was present.

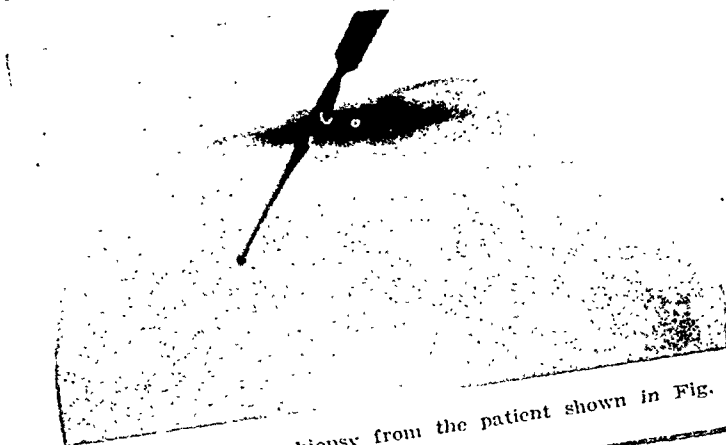


Fig. 12.—Taking the biopsy from the patient shown in Fig. 11.

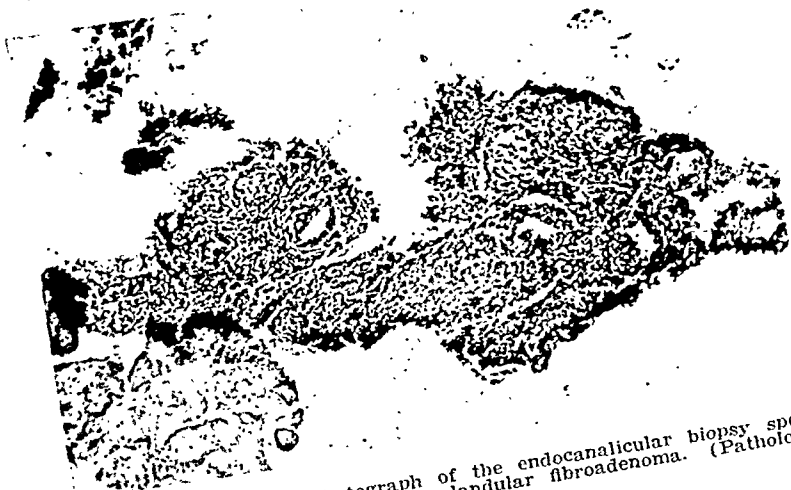


Fig. 13.—Topographic microphotograph of the endocanalicular biopsy specimen of patient of Figs. 11 and 12; papillary and glandular fibroadenoma. (Pathologic study Professor Carlos M. Domínguez.)

This method will often enable the surgeon to operate sooner in cancer of the breast, and to perform small, conservative, prophylactic operations in simple intraductal papillomas which have been well localized.



Fig. 14.—Various filling defects in a milk duct, caused by intraductal growths in a woman with a two-month bleeding from the nipple. There was an indurated milk duct with a small subareolar nodule.

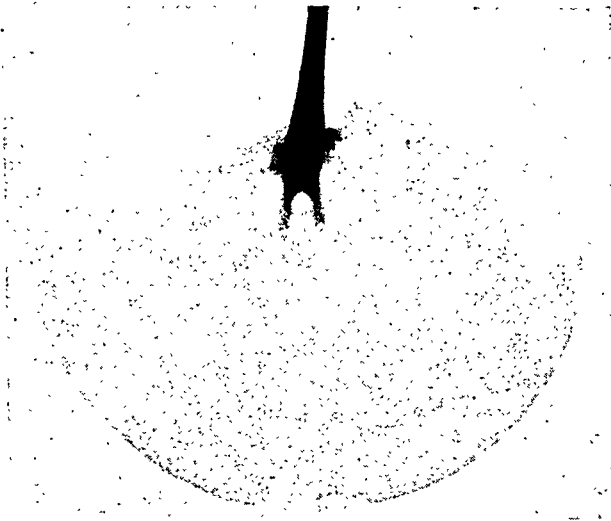


Fig. 15.



Fig. 16.

Fig. 15.—Introduction of a small forceps in the milk duct, in the same patient. Histologic study of the biopsy specimen by Professor Carlos M. Dominguez showed very extended fibroepithelial proliferation accompanied by abundant hemorrhage. The epithelial study revealed, in certain papillary formations, atypical cells and detachment of fusiform cellular sprouts. There were sufficient anatomic proofs to lead one to believe in the malignant transformation of the intraductal fibroadenoma.

Fig. 16.—Incorrect technique, when injecting opaque substance in a milk duct, may permit an air bubble and simulate an intraductal growth.

The pathologic process is localized exactly by introducing into the milk duct a fine metal catheter the extremity of which (by radiographic control) is put in contact with the lesion; then the surgeon can extirpate the corresponding region without searching for, or following, the milk duct. This localizes the site of the lesion, while Babcock's technique localizes the affected milk duct.

As to palpable tumoral lesions, there undoubtedly exist simpler ways of obtaining biopsies. But sometimes, as in high ductal obstructions caused by originally extraductal lesions, this method may also be employed, because, when well executed, it is innocuous, practically painless, and the x-rays aid in selecting the site for the biopsy.

It should be added that subsequent to this work, Felix Leborgne conceived the idea of performing an endocanalicular endoscopic study with simple implements devised and made by him, with which it was possible to obtain direct views of the ductal walls. The endoscopic pictures of the normal and pathologic ducts, as well as details of the instruments employed, will be described in a later article.

# SARCOMA OF THE BREAST

## WITH A REPORT OF THIRTY CASES

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SARCOMA is a relatively uncommon neoplasm. The statistical studies of Williams and of Pack and Lefevre are instructive. The former, in an analysis of 13,824 primary neoplasms, found that 9.4 per cent were sarcomas. In 2,419 instances the breast was the site of the primary lesion and, of these, 3.9 per cent were sarcomas. Pack and Lefevre, in an analysis of 16,565 malignant tumors seen at the Memorial Hospital over a period of twelve years (1917 to 1929), concluded that sarcomas comprised 10.4 per cent of this total and that sarcoma of the breast formed only 0.64 per cent of all breast tumors.

There is considerable variation in the figures for the incidence of breast sarcoma given by different authors. Geist and Wilensky reported 3.9 per cent of all the breast tumors and 7.7 per cent of the malignant breast tumors in their cases to be sarcomas. Deaver and McFarland found 2 per cent of all the breast tumors in their series to be sarcoma. Fox stated that sarcoma represented 3 per cent of all the malignant breast tumors in his series and Hill and Stout reported 1.2 per cent as the incidence of sarcoma among the malignant breast tumors that they studied. The latter authors stated that if adeno-sarcoma were eliminated from their statistics, true sarcoma would comprise only 0.4 per cent of the malignant mammary growths in the series.

From 1926 to 1944 inclusive, 5,499 examples of malignant breast tumor were seen at the Memorial Hospital. Of these, thirty, or 0.5 per cent, were sarcomas. The higher percentage of sarcoma found by the earlier investigators may possibly be due to the inclusion of some small round-cell and spindle-cell neoplasms which, as Ewing has stated, were formerly classified as sarcomas but were in all probability atypical carcinomas.

Williams' statistics would also indicate that the relative liability of the female breast to sarcoma is much below the average for the body in general, 9.4 per cent of the body neoplasms being sarcomatous whereas only 3.9 per cent of female breast neoplasms are of this nature.

The infrequency of the involvement of the breast by sarcoma is further demonstrated by a review of the literature. In 1887, Gross collected 156 cases including 19 of his own, and in 1894, Williams found 99 examples of breast sarcoma in the material he studied. A most extensive survey undertaken by Geist and Wilensky, in 1915, disclosed 433 cases which had been reported since 1858, to which they added 22 of their own. D'Aunoy and Wright, in 1930, and Schreiner and Thibaudeau, in 1932, collected additional examples bringing the total up to 510. Since then, in addition to a number of isolated cases in

the literature, there have been several relatively large series reported (Fox, Rose, Sailer, Rogers and Flo, and Hill and Stout).

The thirty examples of breast sarcoma seen at the Memorial Hospital since 1926 are herewith reported. Since treatment and prognosis are the primary considerations of the surgeon, the emphasis in the present investigation is on these aspects of the subject. The types of sarcoma encountered in the breast, which are to be discussed in the following pages, are enumerated in Table I.

TABLE I. SARCOMA DISCUSSED IN THIS REPORT\*

TYPE	NUMBER
Cysto-sarcoma phyllodes (malignant)	4
Adenosarcoma	1
Fibrosarcoma	2
Spindle-cell sarcoma	5
Angiosarcoma	3
Liposarcoma	4
Lymphosarcoma	7
Hodgkin's sarcoma	2
Carcinosarcoma	1
Myosarcoma	1
Total	30

\*Since this report was prepared, three additional cases of cystosarcoma phyllodes undergoing malignant changes in the stroma have been encountered as well as another example of adenosarcoma.

The sarcomas found in the breast consist of an admixture of epithelial and connective tissue. The epithelial elements are derived from the cells lining the ducts and acini, whereas the mesodermal component originates in either the connective tissue lying beneath the epithelial cells, the subepithelial connective tissue, or in that surrounding the ducts and acini, the pericanalicular and periacinar connective tissue. Hyperplastic changes in the subepithelial connective tissue may give rise to the so-called intracanalicular fibroadenoma, whereas hyperplasia involving the supporting connective tissue between the ducts produces the pericanalicular fibroadenoma.

It is accepted by numerous investigators that many sarcomas and an occasional carcinoma may arise on the basis of a previously existent fibroadenoma. In the course of the development of some sarcomas, the connective tissue elements may obliterate the epithelial components producing an almost pure sarcoma such as the fibrous and spindle-cell varieties. In others the epithelial elements may persist and both structures may manifest malignant characteristics, as in cystosarcoma phyllodes and adenosarcoma. The sarcomas containing both ectodermal and mesodermal constituents will be considered first.

#### CYSTOSARCOMA PHYLLODES

Cystosarcoma phyllodes was first described as a neoplastic entity by Johannes Müller in 1838. In its advanced state it is a huge freely movable tumor which may be cystic in part or solid with small clefts here and there into which project polypoid excrescences (Fig. 1). According to Lee and Pack this tumor develops from a previously existent fibroadenoma, probably of the intracanalicular variety. Lactation may be a factor in initiating this metamorphosis. The history is usually that of a pre-existent nodule which, after many

years of inactivity suddenly begins to increase in size. In some instances this is apparently initiated by trauma. Pain and ulceration may occur in the late stages after the tumor has become very large.

This neoplasm is usually benign but in some instances a true sarcomatous transformation takes place characterized by stroma proliferation, the presence

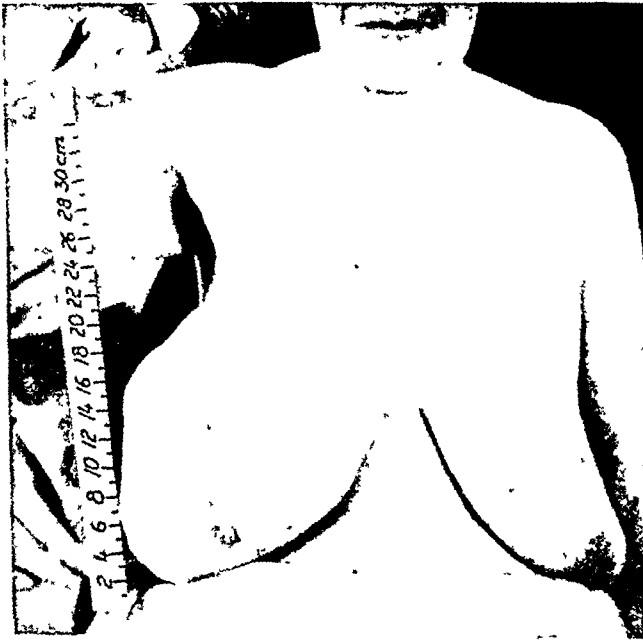


Fig. 1.—Cystosarcoma phyllodes.



Fig. 2.—Photomicrograph of cystosarcoma phyllodes showing stroma proliferation, mitotic figures, and atypical cells ( $\times 340$ ).

of mitotic figures, and of atypical cells (Fig. 2). In other instances there may be a metaplasia of the stroma resulting in myxomatous change or occasionally in squamous metaplasia with the formation of epithelial pearls.

Although these tumors are of low-grade malignancy, local recurrences and even distant metastases with fatal termination are sometimes encountered. Examples of this have been observed (Prym, Sophian, and White). Recently Cooper and Ackerman reported a unique case in which the axillary nodes were involved by metastasis of the connective tissue component.

During the period of 1926 to 1944, inclusive, there were seen at the Memorial Hospital forty-five examples of cystosarcoma phyllodes of which four, or 8.8 per cent, revealed sarcomatous metamorphosis. The metaplasia involved only the connective tissue. Of these patients with malignant deviation of the lesion, two underwent simple, and two radical, mastectomy. One of the latter patients was free of disease seven and one-half years after operation and the other was free of disease when last seen one year after mastectomy. Of the patients who underwent a simple mastectomy, one was lost to follow-up and the other was apparently free of disease one year after operation.

#### ADENOSARCOMA

Adenosarcoma is the malignant variant of fibroadenoma composed of both epithelial and connective tissue elements which is thought to arise in the pericanalicular variety. Many of these tumors result from the transformation of a long-standing fibroadenoma in which gestation, lactation, or trauma may have been an initiating factor. The history is that of a rapidly growing tumor which may ultimately occupy most of the breast. These tumors may be rounded or lobulated and composed of solid or cystic elements, some of the latter often attaining a huge size. In the initial stages the tumor is well circumscribed but as growth progresses it may spread out into the breast and fungate through the skin.

Although the microscopic structure is varied, the majority of these tumors are composed of spindle cells surrounding the acini and ducts. The epithelial component may manifest growth activity in the early phases but it is later, for the most part, obliterated by the connective tissue elements.

This type of neoplasm, according to Ewing, is highly malignant and although remissions have been observed the course is usually progressive with, in many instances, a rapidly fatal termination. As the tumor grows it involves the overlying skin, the pressure causing ulceration and necrosis with consequent sepsis and death. In some instances a fatal termination of the disease may result from metastasis. Local recurrences after removal of the tumor are frequent and, as Finsterer has shown, they may take the form of a spindle-cell sarcoma.

There was one example of adenosarcoma in this series. The patient was treated by simple mastectomy and low axillary dissection followed by a course of x-ray therapy. After remaining free of evidence of disease for twelve years she developed pulmonary metastases, proved by bronchoscopy, and died.

## FIBROSARCOMA AND SPINDLE-CELL SARCOMA

Among our patients, as with those of other investigators, the fibrosarcomas and spindle-cell sarcomas constituted the numerically largest group. In the present series seven cases, or 23 per cent of the total, were in that category. In the experience of other observers these tumors constitute from 25 to 70 per cent of all breast sarcomas. Fibrosarcoma and spindle-cell sarcoma may arise in any location where there is supporting connective tissue. In addition, they may originate in the breast from a pre-existent fibroadenoma. The fibrosarcomas are relatively benign, whereas the spindle-cell tumors vary considerably in their degree of malignancy. Those composed of small cells are slower growing, relatively benign, and approach in structure and clinical features the fibrosarcomas.

Those composed of large cells exhibit more active growth, are softer, more vascular, tend to ulcerate and become necrotic. They metastasize and are prone to local recurrence. As this type of tumor grows it may infiltrate the surrounding tissues and structures, frequently penetrating blood vessels, thus producing metastases. These tumors grow relatively slowly in comparison with other forms of breast sarcoma and do not reach a large size.

In our series there were five spindle-cell sarcomas and two fibrosarcomas. All appeared to be of low-grade malignancy. One of the fibrosarcomas and one of the spindle-cell sarcomas were thought to have had their origin in a pre-existing fibroadenoma. The operative procedure in these cases was a simple mastectomy or local excision of the tumor, except in one instance in which a radical mastectomy was performed. This patient died six months after operation. One of the patients subjected to a simple mastectomy developed recurrences in the chest wall, dying five months after operation. One patient, treated by irradiation because she refused surgery, was lost to follow-up. The end result for this group of cases is shown in Table II.

Although not arising in the breast, two unusual examples of connective tissue tumors appearing in this organ are briefly mentioned here. The first was

TABLE II. COMPARISON OF THE RESULTS FOLLOWING RADICAL AND CONSERVATIVE SURGERY FOR FIBROSARCOMA AND SPINDLE-CELL SARCOMA ON THE BASIS OF FIVE-YEAR SURVIVAL

AUTHOR	RADICAL MASTECTOMY		SIMPLE MASTECTOMY OR LOCAL EXCISION		AXILLARY NODE INVOLVEMENT	
	ALIVE	DEAD	ALIVE	DEAD	ALIVE	DEAD*
Adair and Herrmann		1	4	1		
Boldrey	1		1			
Finsterer		1	3	2		1
Fox	9	4	5	6	1†	1
Hill and Stout	1	2	1	1		
Rogers and Flo	3		6	3		
Sailer	1	3				1
Schreiner and Thibaudeau	1	1		2		
Warren and Meyer	1†	1				
Total	17	13	20	15	1	3

\*All deaths with node involvement occurred within twelve months following surgery.

†Alive six years but has recurrent nodules and liver has begun to enlarge.

‡No follow up.



that of a 60-year-old woman with a soft, freely movable tumor 2 cm. in diameter in the right breast, of one week's duration. A radical mastectomy was performed. The tumor was found to lie immediately over the pectoralis muscle and to infiltrate it. The microscopic diagnosis was spindle-cell sarcoma, probably fascial—nodes clear.

The second case was that of a 32-year-old woman who, a few months after the birth of her only child, noticed a lump in the upper inner quadrant of the left breast. This increased in size over a period of eight months, at which time it measured about 2 cm. Skin dimpling could be developed over it. One small node was palpable in the left axilla. At operation a firm mass extending into the underlying pectoralis muscle was found which was widely excised with the surrounding muscle tissue. The microscopic diagnosis was desmoid. In so far as it is not unusual to encounter areas of fibrosarcomatous and myxosarcomatous transformation in desmoids (Pack and Ehrlich), the case is mentioned although no sarcomatous changes were noted in this example.

#### ANGIOSARCOMA

Blood vessel tumors, although a relatively common type of neoplasm, rarely undergo malignant deviation. An occasional angioma may metastasize following trauma, but according to Geschickter and Keasby less than 1 per cent of benign angiomas subjected to treatment manifest malignant changes.

Angiomas associated with metastases fall into three groups. In the first the primary lesion may be benign and produce benign-appearing metastases (Borrmann). In the second group an apparently benign angioma gives rise to malignant metastases (Robinson and Castleman). The third group comprises those cases in which the initial lesion, as well as the metastases, exhibits malignant characteristics (DaCosta, and Menville and Bloodgood). It is thought by some observers that those instances in which both primary and metastatic foci appear benign are really examples of a multicentric origin rather than of a metastatic phenomenon.

The clinical history of breast angiosarcoma is that of a tumor which, in the course of a few months, grows to a large size. Occasionally a purplish hue is imparted to the skin by the underlying tumor but usually there are no characteristic physical features associated with this neoplasm. The youth of the patient is suggestive although this neoplasm has been reported in elderly people.

In our series there were three examples of angiosarcoma, one of which is illustrated by Figs. 3 and 4. The ages of these women were 21, 23, and 26 years, respectively, an average of 23 years and 4 months. One patient underwent a radical mastectomy, one a simple mastectomy, and the third a local excision of the tumor. All died of the disease. The progress in this disease is relatively rapid, the average duration of life after operation in our patients being twenty-eight months. The two patients reported by Rogers and Flo died six months and two years, respectively, following simple mastectomy. In the cases reported by Hill and Stout the patients succumbed soon after operation, one three

months after simple mastectomy and the other about six weeks following a radical procedure. It would appear that metastasis occurs early. In two of our patients this phenomenon was encountered six and eight months, respectively, after the removal of the tumor. In one case reported by Hill and Stout metastatic disease appeared in the lungs one month after radical mastectomy.

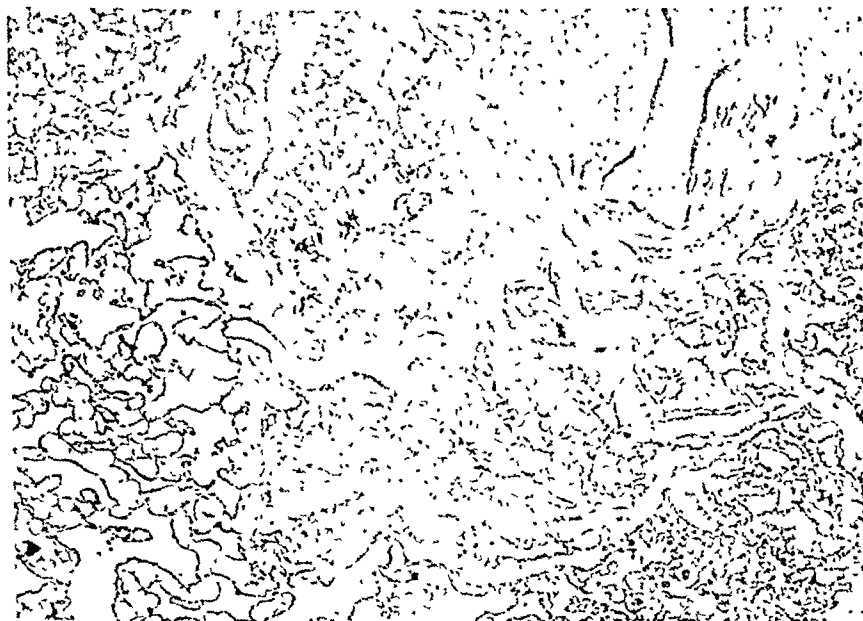


Fig. 3.—Photomicrograph of angiosarcoma; at the upper right a breast duct may be seen, at the left is normal-appearing angioma, and at the right angiosarcoma ( $\times 80$ ).



Fig. 4.—Higher magnification of the area of angiosarcoma shown in the preceding photograph ( $\times 300$ ).

Geschiekter mentioned two cases, one with axillary node invasion in a 53-year-old woman and the other with widespread metastasis in an elderly woman. On the other hand, the patient of Menville and Bloodgood, a 53-year-old woman, lived 10 years without evidence of the disease, following a radical mastectomy.

Many of the symptoms encountered in the course of this disease are due to hemorrhage from the metastatic foci. One of our patients developed hemiplegia and, some time later, an abdominal crisis associated with abdominal pain, rigidity, and shock, from which she did not recover. These phenomena were undoubtedly the result of hemorrhage from metastatic foci. The second patient developed pulmonary metastases and the third, metastases to the spine, pelvis, femur, sternum, and liver. Because it is a blood vessel tumor, metastasis by the vascular route in all probability occurs early and for that reason the prognosis is poor. Internal hemorrhage is frequently the cause of death.

#### LIPOSARCOMA

Liposarcoma is encountered most frequently in the retroperitoneal fat and in the extremities but it may be found in other parts of the body. Its occurrence in the breast, however, is unusual. Lifvendahl, in 1930, reported a fatal case occurring in a lactating woman. He was unable to find any other reported case of breast liposarcoma. Schultz-Brauns (1933) remarked on the rarity of the condition and Fox, in 1934, included one example of breast liposarcoma in his report of sixty mammary sarcomas. The patient was free from evidence of disease six months after a radical mastectomy. Geschiekter (1940) mentioned three liposarcomas of the breast but gave no details.

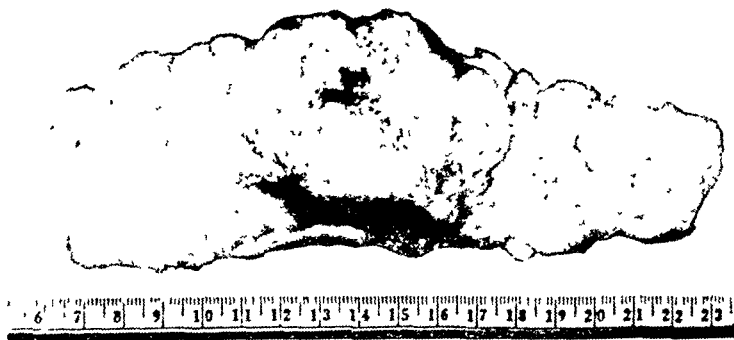


Fig. 5.—Gross appearance of liposarcoma of the breast.

There were four instances of this variety of sarcoma in our present series. The gross and microscopic appearance of one of these tumors is shown in Figs. 5 and 6. One patient with a grade 4 liposarcoma had associated lymphatic leucemia. She was free of evidence of sarcoma four months after a radical mastectomy. The others were myxoliposarcomas of low-grade malignancy. One underwent a simple mastectomy followed by numerous recurrences over a period of ten years. She died ultimately of pulmonary metastasis. Of the other two patients, one had a local excision of the tumor, the other a radical mastectomy, and both have been free of disease four and four one-half years, respectively.

Seids and McGinnis believed that the high degree of malignancy of retro-peritoneal liposarcoma may be due to the technical difficulties of removing all of the surrounding fat. If that be valid then the prognosis should be better for liposarcoma of the breast because here the lesion and contiguous fat are better circumscribed and readily extirpated with the breast.

#### LYMPHOSARCOMA AND HODGKIN'S SARCOMA

During the interval covered by the present survey, seven instances of primary lymphosarcoma of the breast were encountered at the Memorial Hospital. There is nothing characteristic about the lesion in this location by which a preoperative diagnosis can be established, although aspiration biopsy in some cases is suggestive. Clinically, the lesion resembles carcinoma. A radical mastectomy was performed in three instances, a simple mastectomy in one, and a local excision in the others. All patients were alive and free from disease over periods ranging from several months to seven years. Some of these cases have been reported in detail elsewhere (Adair and Herrmann).

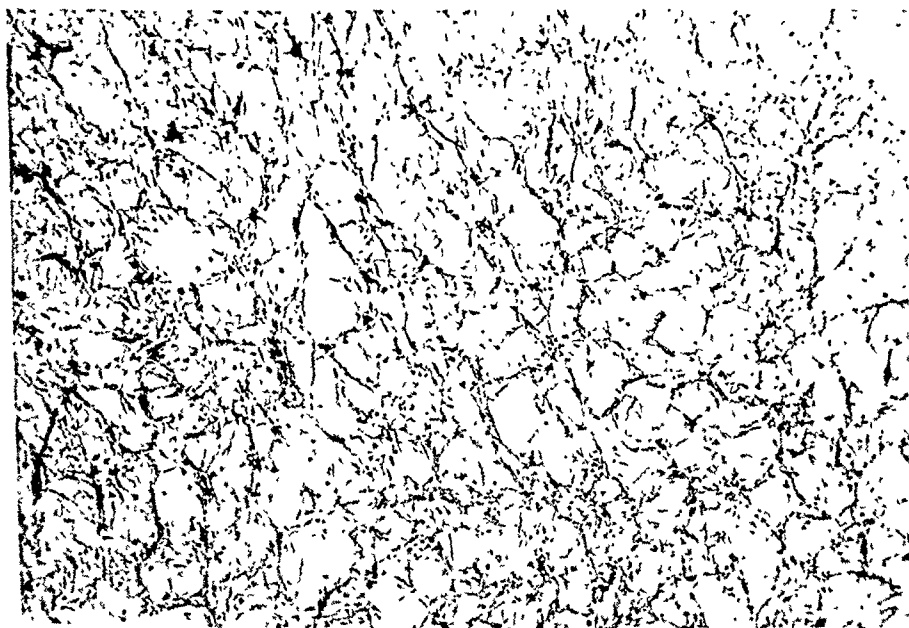


Fig. 6.—Photomicrograph of liposarcoma ( $\times 240$ ).

Also during this period two patients with probable primary Hodgkin's disease of the breast were studied and have been described in another communication (Adair, Craver, and Herrmann).

#### CARCINOSARCOMA

This neoplasm is composed of both carcinoma and sarcoma. A number of examples have been reported. There was one in the present group of cases. Several theories have been advanced to explain the presence of carcinoma and sarcoma in the same neoplasm:

1. That it is a mixed tumor.
2. That a carcinoma stimulates the adjacent connective tissue to undergo sarcomatous transformation or, conversely, that an antecedent sarcoma causes a carcinomatous change in the neighboring epithelial elements.
3. That there are two distinct and separate tumors which grow toward each other and coalesce.
4. That the lesion is a primary carcinoma, some portions of which become so altered in histologic appearance that they are interpreted as sarcoma (Saphir and Vass).

Our patient had a small tumor in the breast for eighteen years, which for the last two years had grown rapidly. It was removed but recurred one and one-half years later. A modified radical mastectomy was then performed. It appeared on pathologic examination that the malignant process had its inception in a giant intracanalicular fibroadenoma. There was no lymph node involvement. She died of pulmonary metastasis five months after operation.

Other examples of sarcoma composed of more than one element are occasionally encountered in the breast. Two of these are the osteosarcoma and chondrosarcoma. Whether the osseous and cartilaginous foci arise from embryonic rests or as a result of metaplasia is a moot point. These tumors appear to be of relatively low-grade malignancy. There were no examples of these neoplasms in the present series.

#### MYOSARCOMA

Myosarcoma is an unusual tumor of the breast which may originate from smooth or striated muscle. Several cases have been reported (Bérard and associates, Leroux and Chanton, Geschickter, and Sailer). There was one example of an angiomysarcoma in the present series. The therapeutic procedure in this instance was a local excision of the tumor. The subsequent course is unknown because the patient failed to report back to the clinic.

#### DIAGNOSIS

The diagnosis of breast sarcoma in most instances necessitates the differentiation of this condition from cyst or carcinoma. The history is frequently suggestive of sarcoma. In these instances the patient states that a tumor has been present, although quiescent, for a considerable length of time. Suddenly it begins to increase rapidly in size. This occasionally follows a trauma. A cyst may exhibit the same phenomena although in the latter condition there is rarely the history of a pre-existent tumor. The spherical, cystic property of the mass and its capacity to transilluminate suggest that the tumor may be a cyst. Sarcoma is not translucent except in those forms of cystosarcoma phylloides which are more cystic than solid.

Carcinoma may be suspected if there is skin dimpling or nipple retraction. These are seldom observed in sarcoma unless the tumor becomes so large that it impinges on the overlying skin. Then it may produce attachment, redness, and ulceration. Occasionally a diffuse duct carcinoma may produce great enlarge-

ment of the breast and in this respect simulate sarcoma. However, the diagnosis of sarcoma may be difficult or impossible to establish by clinical means. Aspiration biopsy in most instances will furnish the requisite information.

#### METASTASIS

Sarcomas are usually very vascular. Some of the blood vessels are present before the tumor undergoes sarcomatous transformation, but the greater number are newly formed to meet the requirements of the rapidly growing neoplasm. These channels are lined by a single layer of cells which is all that separates the lumen from the tumor. The neoplastic cells may penetrate the wall of the blood channel to form a parietal thrombus which may be broken off and carried as a tumor embolus to the lung to produce a metastatic focus. There is metastasis to distant organs in 12 to 18 per cent of the cases. In order of frequency these are lung, liver, brain, dura mater, pleura, mediastinal, retroperitoneal, and axillary nodes, heart, kidney, and bones (Geist and Wilensky, Cheatele and Cutler). In our series there were lung metastases from a carcinosarcoma, a spindle-cell sarcoma, a myxoliposarcoma, and an angiosarcoma. Another angiosarcoma metastasized to the bones and liver. Despite an apparent cure of a breast sarcoma it is possible for a metastatic focus to appear after many years. This, however, is an unusual phenomenon. Willis quoted several examples, all of pulmonary metastasis but from sarcoma other than mammary. In one of our patients, lung metastasis appeared twelve years after a simple mastectomy for spindle-cell sarcoma, the patient having remained free from evidence of the disease during the interim. Whenever long-delayed metastasis occurs under these circumstances it would seem that the secondary lesion must have had its inception before the local neoplasm was removed. After lying dormant for a lengthy period of time these cell emboli manifest growth activity for some reason, either stimulation or removal of inhibition.

Lymphatic channels have not been described in sarcoma. For this reason the lymphatic spread of the disease with invasion of the lymph nodes, except in lymphosarcoma, melanosarcoma, and carcinosarcoma, is necessarily a rare phenomenon.

Although axillary and supraclavicular lymph nodes may be palpable, the enlargement in most instances is the result of an inflammatory rather than a metastatic process. In our series four patients had palpable axillary nodes. Three underwent a radical procedure and no involvement of the nodes was found. There was a local excision of the tumor without removal of nodes in the fourth patient. In two additional patients with no palpable adenopathy, hyperplastic nodes were encountered at operation. Upon microscopic examination these were found to be free of disease.

Metastatic lymphatic spread in sarcoma, although infrequent, has been observed. Gross gave the incidence of axillary involvement as 0.64 per cent. Poulsen found axillary node disease in three instances among thirty-three patients, an incidence of 9 per cent. Geist and Wilensky in a collection of 435 cases found 3 per cent of the patients to have lymph node invasion. In Table III there has been assembled 678 examples of breast sarcoma taken from

TABLE III. LYMPH NODE INVOLVEMENT IN REPORTED CASES OF BREAST SARCOMA

AUTHOR	YEAR	NUMBER OF CASES	NUMBER WITH LYMPH NODE METASTASE :
Geist and Wilensky	1915	435	13
D' Aunoy and Wright	1930	68	4
Sophian	1930	15	0
Schreiner and Thibaudau	1932	7	0
Fox	1934	52	2
Rose	1936	15	1*
Sailer	1937	15	1
Harrington and Miller	1940	9	0
Hill and Stout	1942	10	0
Rogers and Flo	1942	22	1
Adair and Herrmann	1945	30	0
Total		678	22 (3.2%)

\*Melanosarcoma.

the literature. No attempt has been made to collect all the individual case reports. Only the relatively large series have been included. It is seen that among this group there are twenty-two instances of lymph node metastasis, one of which was in association with a melanosarcoma. This does not mean that 3.2 per cent of the patients with breast sarcoma have lymph node disease but merely that in this collected series the reported examples of lymph node invasion constitute 3.2 per cent of the total number of reported cases. It is possible that the actual incidence of node involvement is smaller than appears from the figures because in some of the earlier examples the primary lesion may have been a round-cell or spindle-cell carcinoma which, as Ewing has stated, was frequently confused with sarcoma. Geist and Wilensky remarked that in their series most instances of lymph node involvement occurred with the round-cell type of tumor.

It is of interest that all of the patients with fibrosarcoma or spindle-cell sarcoma in whom lymph node metastasis was found, and in whom the progress of the disease could be determined (Table II), succumbed to the malady within one year after operation. Although no accurate conclusions can be derived from this small number of instances, it suggests that, if the axillary nodes are diseased, the prognosis is decidedly grave, much more so than in carcinoma of the breast with axillary metastasis. The explanation may be that the node involvement, as Stewart and Copeland have suggested for neurogenic sarcoma, is produced by venous tumor emboli. On that basis, metastasis to the nodes is merely one aspect of a general blood-borne dissemination of the neoplasm.

#### SURGICAL THERAPY

Many authors (Geist and Wilensky, Cheate and Cutler, Deaver and McFarland, Rose) advocate radical mastectomy as the procedure most likely to produce the highest cure rate. In so far as it has been demonstrated that there are different varieties of sarcoma which vary in degree of malignancy and since there are variations within the individual groups, it would seem that such a sweeping conclusion is unwarranted.

In an endeavor to evaluate the efficacy of the surgical procedures employed in the treatment of sarcoma, sixty-five suitable cases of fibrosarcoma and spindle-cell sarcoma, were selected for analysis. These varieties were chosen

because they constitute the numerically largest group of sarcomas. Only those patients who were living and free from disease five years or longer after operation were chosen for comparison with those who had undergone surgery and died from the disease within that period. The compilation of such a group presents several difficulties. In the first place many cases are unsuitable because they are reported so soon after operation that there is no opportunity to know the postoperative course. In others the follow-up period is less than five years. Another difficulty encountered is that a great number of sarcomas were treated in the period before the radical procedure was introduced by Halstead (1893). Therefore, in order to evaluate this factor properly, only those patients who were treated after 1893 were considered.

The results have been tabulated (Table II). It is seen that of thirty patients who were subjected to radical mastectomy seventeen are alive and thirteen are dead, and of thirty-five who underwent a simple mastectomy or local excision twenty are alive and fifteen are dead. The parallelism between the number of deaths in the two groups (radical and simple mastectomy) is more significant than that of the survivals in the corresponding series for the following reason. The deaths all occurred within three years after operation, the majority within a much shorter period. The possibility for accurate follow-up is much greater over a relatively short period than it is for a longer one. Patients who have recurrence of the disease are much more likely to report back to the clinic than those who are well. Thus, the large majority of those who fail to return are undoubtedly free of disease and should be included among those cured by operation. When considered in this light the very small proportion of cured sarcomas in Table II loses its apparent significance. From this small series one cannot draw accurate conclusions but it does suggest that the simple mastectomy is as effective as the radical procedure in the treatment of fibrosarcoma and spindle-cell sarcoma.

As a further aid in evaluating the therapeutic procedure of radical mastectomy it was thought that the presence or absence of axillary node involvement in patients so treated might furnish an index. One hundred cases in which a radical mastectomy was performed were gathered from the literature. Only examples of lymphosarcoma, melanosarcoma, and carcinosarcoma were excluded because these forms of sarcoma behave like carcinoma and metastasize chiefly by way of the lymphatics. The collected cases have been tabulated according to authors (Table IV) and according to type (Table V). It is seen that 4 per cent of these patients had axillary node disease. Although the value for statistical analysis of this small series is limited, it would seem that lymph node involvement in breast sarcoma is too infrequent to justify the employment of radical surgery. Furthermore, some of the examples of lymph node involvement may be on the basis of mistaken diagnosis of the primary lesion and others may be the result of venous embolism. If there are tumor emboli in the blood stream, removal of the regional lymph nodes would seem to be of little value.

On the other hand, Warren and Meyer concluded from their studies of sarcoma in various anatomic locations that lymph node metastasis occurs in



TABLE IV. LYMPH NODE INVOLVEMENT IN ONE HUNDRED COLLECTED CASES OF BREAST SARCOMA; TREATMENT BY RADICAL MASTECTOMY

AUTHOR	NUMBER OF CASES	NUMBER OF CASES WITH AXILLARY NODE DISEASE
Adair and Herrmann	6	0
Bishop	2	0
Boldrey	1	0
D' Aunoy and Wright	4	0
Fox	23	2
Geist and Wilensky	11	1
Harrington and Miller	9	0
Hill and Stout	11	0
Menville and Bloodgood	1	0
Rhodenberg	6	0
Rogers and Flo	4	0
Rose	9	0
Sailer	7	1
Schreiner and Thibaudau	2	0
Sophian	2	0
Sullivan	1	0
Wellbrock	1	0
Total	100	4

In a few instances in which the nodes were not mentioned it is assumed that they were uninvolved.

about 7 per cent of cases exclusive of melanosarcoma and lymphosarcoma. They believed that lymph node dissection in conjunction with radical removal of the sarcoma may improve the prognosis from 5 to 10 per cent and may be of value even after lymphatic metastasis is clinically evident. This is not substantiated for breast sarcoma by the present investigation.

There are, however, three types of breast sarcoma in which radical mastectomy appears to be indicated. One is the so-called carcinosarcoma, another is melanosarcoma, and the third, as we have suggested in a previous communication, is lymphosarcoma primary in the breast. In lymphosarcoma and melanosarcoma the mode of spread is thought to be almost entirely by way of the lymphatics.

TABLE V. TYPES OF SARCOMA AND ASSOCIATED LYMPH NODE INVOLVEMENT IN 100 CASES; TREATMENT BY RADICAL MASTECTOMY

TYPE OF SARCOMA	NUMBER OF CASES	NUMBER WITH LYMPH NODE INVOLVEMENT
Fibrosarcoma	44	3
Spindle-cell	12	
Adenofibrosarcoma	9	
Cystosarcoma	7	
Liposarcoma	4	
Round-cell	4	1
Unknown	4	
Neurogenic	3	
Angiosarcoma	3	
Perithelioma	3	
"Sarcoma"	3	
Polymorphous cell	2	
Osteochondrosarcoma	1	
Giant cell	1	
Total	100	4

In carcinosarcoma the epithelial component may metastasize to the regional nodes as it does from carcinoma of the breast. In Smithy's collected group of thirty-three cases, twelve, or 36 per cent, revealed axillary node metastasis of the epithelial element. This approximates the figure (33 per cent) that Harrington and Miller gave for the incidence of axillary node involvement in cases of breast cancer with no palpable axillary nodes.

Aside from the exceptions just noted, we believe from the available evidence that conservative surgery in breast sarcoma produces as satisfactory a result as does the radical procedure with none of the disadvantages of the latter. Since there is evidence that breast sarcoma owes its inception in some instances to malignant deviation of a fibroadenoma this tumor should be removed early. Early removal is also the best method for preventing metastatic spread if sarcomatous change has already occurred. If the tumor is small and of low-grade malignancy, simple excision should suffice. If larger or of a higher degree of malignancy a simple mastectomy with removal of the pectoral fascia is indicated. The more malignant forms have the tendency to infiltrate the underlying muscle and give rise to recurrences. For that reason, in situations where there is evidence of this possibility the pectoralis major muscle should be removed. Fox advocated removal of both pectoral muscles in all cases but omitted an axillary dissection. Geschickter, on the other hand, favored simple mastectomy with the removal of the pectoralis fascia in the treatment of fibrosarcoma and spindle-cell sarcoma.

It is of interest that the present-day conclusions concerning the surgical treatment of breast sarcoma coincide with those arrived at by Gross before the era of radical surgery. In 1887 he wrote, "The entire breast along with any skin that may be invaded must be extirpated, especial care being paid to the complete removal of every particle of paramammary fat and the fascia of the pectoralis muscle, in which tissues experience shows that recurrence takes place."

#### RADIATION THERAPY

The radiosensitivity of tumors varies. Among sarcomas the lymphosarcoma and Hodgkin's sarcoma are relatively sensitive. Liposarcomas also show some sensitivity but there is considerable variability. The types composed of young fat cells and those that contain mucoid and myxosarcomatous areas tend to be relatively sensitive to large doses of x-rays. Those composed mainly of adult spindle cells are more resistant.

Since breast sarcoma is an unusual lesion there has been relatively little opportunity to determine the therapeutic effect of irradiation on these tumors. Wintz reported thirteen patients, most of them with spindle-cell sarcomas treated by this modality. Four received preoperative x-ray therapy and then underwent a cautery excision of the tumor. In addition, three of these individuals were subjected to x-ray castration. These patients were alive after twenty, thirteen, and seven years, respectively. The fourth, or noncastrated patient, was free of disease for two years, at which time she became pregnant. In the first month of the pregnancy she developed a recurrent nodule in the breast followed soon

after by widespread skin nodules, lung metastasis, and death. Wintz believed it significant that this patient was not castrated.

One patient was subjected to a radical mastectomy followed by x-ray therapy. Two years later she developed a recurrence and died shortly thereafter of lung metastasis. Four inoperable tumors were treated by irradiation, all of the patients dying within two years following initiation of this therapy. Of four patients with recurrence after operation treated by irradiation, three died within the first year and the other during the second year postirradiation.

Wintz concluded that preoperative irradiation is of value in those instances in which the sarcoma is confined to the breast but that x-ray therapy is useless in those cases in which the process has spread beyond its confines or in recurrent disease.

Some investigators have reported favorable results from irradiation. Pfahler was enthusiastic about this agent especially in the treatment of recurrences. It is possible, however, that in some of the instances in which spectacular regression of the lesion is achieved the neoplasms may be lymphosarcoma or small cell carcinoma.

Geschiekter believed that for liposarcoma, irradiation is preferable to radical surgery but that at best the disease can only be arrested, not cured. He advocated irradiating the regional lymph node areas as well as the breast because of the possibility of metastasis.

Lymphomatous involvement of the breast is infrequent but where it does occur it is usually as a local manifestation of a generalized disease process. Under these conditions palliative x-ray therapy is the treatment of choice.

Roentgen therapy was administered to six of our patients. Two individuals with fibrosarcoma and one with spindle-cell sarcoma were irradiated following simple mastectomy. They were all alive and free of disease for more than nine years after operation. One woman with a spindle-cell sarcoma received x-ray therapy and gold radon seeds but refused operation and was lost to follow-up.

One of our patients with angiosarcoma underwent a radical mastectomy and postoperative x-ray therapy. She died of pulmonary metastasis two years after the initial appearance of the breast tumor. Another woman with adenosarcoma underwent a modified radical mastectomy and postoperative high voltage roentgen therapy. She remained free of disease for twelve years, after which she developed lung metastasis and died.

From this small number of cases no accurate conclusions may be established. In those long-surviving patients whose lesion was a sarcoma of low-grade malignancy and in whom a simple mastectomy followed by irradiation were the therapeutic procedures, it is conceivable that surgery alone might have sufficed. This reasoning may also apply in the three cases of preoperative irradiation followed by local excision reported by Wintz. In our two instances of highly malignant sarcoma the patients died of the disease despite radical surgery and associated x-ray therapy.

Postoperative x-ray treatment, however, may be of value in very cellular tumors and in those which manifest infiltrative tendencies. There is also a pos-

sibility that the vessels adjacent to the excised tumor or breast may contain tumor thrombi. Under these circumstances radiation therapy might prove advantageous.

It is quite possible that in some forms of breast sarcoma the incidence of recurrence and metastasis may be materially decreased by irradiation. Until enough data have been accumulated, a definite conclusion cannot be reached.

#### PROGNOSIS

The prognosis is dependent upon the variety of the neoplasm. Sarcoma is a generic term for a number of new growths which have in common their origin from mesodermal elements. These tumors vary in their malignant potentialities. At one end of the scale is the low-grade malignant variant of cystosarcoma phylloides and at the opposite extreme is the highly malignant angiosarcoma. This classification is subject to further division because there are variations in degree of malignancy within the groups. Thus, prognosis depends not only on the type of sarcoma but also on the grade of the particular lesion within the group.

Age is also a factor. Sarcoma tends to occur in relatively young women. The average age for our patients was 45 years. Gross summarized the influence of age when he wrote, "Sarcoma occurring in a functionally active breast evinces a morbid disposition to recur after operation with less disposition to metastasize whereas a sarcoma of the declining breast recurs less frequently but it generalizes in a greater number of instances." This generalization does not appear to apply to angiosarcoma as evidenced by the rapid appearance of metastases in our youthful patients and those of similar age reported in the literature.

Local recurrence, regardless of the surgical procedure employed, is a frequent occurrence but does not necessarily imply a poor prognosis. For example, Riedel removed recurrent lesions six times over a period of twenty years, the patient exhibiting no evidence of disease at the time of death. A similar experience was reported by Gross. The latter stated that 50 per cent of the recurrences take place within the first six months and that they may appear as late as twenty-five years after the removal of the initial lesion. The high percentage of recurrences given by the earlier writers may have been due to the inclusion of atypical carcinomas among their sarcomas. There were recurrences in eight of the cases being reported. These occurred in the following classes: liposarcoma, spindle-cell sarcoma, carcinosarcoma, and all of the instances of angiosarcoma.

It has been frequently stated that sarcoma of the breast offers a better prognosis than carcinoma in this organ. This, as shown previously, depends upon the variety and grade of the sarcoma. Certainly angiosarcoma is much more malignant than most cancers and, conversely, low-grade fibrosarcoma and liposarcoma are much less malignant than low-grade carcinoma. For that reason a general statement is not valid and prognosis must be determined, not from the disease as a whole, but from an evaluation of each example on the basis of type and histologic grading. Lymph node involvement appears to have a much more serious implication in connection with breast sarcoma than the same phenomenon in association with breast cancer. Death may result from sepsis in those in-

stances where the primary lesion or recurrences break down and ulcerate. In some cases metastasis causes a lethal outcome, whereas in the angiosarcomas internal hemorrhage from a metastatic focus is frequently the cause of death.

#### SUMMARY AND CONCLUSIONS

1. Various types of sarcoma encountered in the breast are briefly described.
2. Thirty cases of breast sarcoma are reported, among which are three angiosarcomas.
3. A study of 100 radical mastectomies for sarcoma reveals lymph node invasion in 4 per cent.
4. An analysis of the results of surgical therapy would indicate that conservative procedures are as effective as radical measures.
5. Radical mastectomy is the procedure of choice in primary lymphosarcoma, melanosarcoma, and carcinosarcoma.
6. There are not enough data on irradiation of breast sarcoma by which to evaluate the efficacy of this therapeutic procedure.

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# A HISTOLOGIC CLASSIFICATION OF CARCINOMA OF THE BREAST\*

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NO UNIFORMLY accepted modern classification of carcinomas of the breast now exists and any effort to construct one becomes an easy object of criticism. To satisfy the justly practical needs of the clinical surgeon and to appease all of the demands of the tumor morphologist together make this problem generally discouraging. Attitudes toward classification differ greatly from person to person and William Boyd, according to N. C. Foot,<sup>1</sup> has divided classifiers into "lumpers" and "splitters," the implications of which need no exposition. We are forced to admit that we employ both the device of lumping and that of splitting. In general, we prefer to split when sufficiently acquainted with particular types of tumors and to lump when the histologic and clinical characters of a group of tumors are not familiarly known or recorded.

With increasing emphasis on the recognition of cancer in its earliest phases, it seems desirable when possible to include in classification schemes a listing for noninfiltrating forms of carcinoma. Whereas the existence of these non-infiltrating forms is being increasingly accepted, there still remains a body of pathologists who will not make the diagnosis of carcinoma unless they detect infiltration. This is scarcely logical since it is so much more reasonable to conclude that if the tumor had not been a carcinoma prior to infiltration, then infiltration would not have occurred. In the classification scheme to follow, in so far as possible, the tumors have been classified as to site of origin and, hence, the nipple has been taken as a point of beginning, followed by tumors of ducts and lobules, and finally certain relatively rare or highly unusual histologic types have been enumerated. Comment as to the probable site of origin of these rare types will be made as each is discussed. The classification to be presented deals only with the various histologic types of mammary carcinoma. Certain forms of mammary cancer such as carcinoma en cuirasse and inflammatory carcinoma are omitted since they do not have histologic specificity. Benign tumors of the breast proper are not to be discussed. It is not one of the purposes to include tumors of the skin of the breast and its appendages or the various tumors of the soft somatic tissues, since these tumors are related to the breast in only a regional sense.

## HISTOLOGIC CLASSIFICATION OF CARCINOMAS OF THE BREAST

- I. Paget's Disease of the Nipple
- II. Carcinomas of Mammary Ducts
  - (a) Noninfiltrating tumors
    - 1. Papillary carcinoma
    - 2. Comedocarcinoma

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\*The authors are presenting this paper by request and as part of a symposium on mammary cancer. They are quite aware of the fact that it contains no new material and justify it solely through the feeling that it may lessen somewhat the confusion common to the classification of carcinomas of the breast. The classification presented, naturally, is that of the Memorial Hospital.

- |                         |   |   |
|-------------------------|---|---|
| (b) Infiltrating tumors | { | <ol style="list-style-type: none"> <li>1. Papillary carcinoma</li> <li>2. Comedocarcinoma</li> <li>3. Carcinoma with productive fibrosis</li> <li>4. Medullary carcinoma</li> <li>5. Colloid carcinoma</li> </ol> |
|-------------------------|---|---|

### III. Carcinomas of Mammary Lobules

- (a) Noninfiltrating
- (b) Infiltrating

### IV. Relatively Rare Carcinomas

1. So-called sweat gland carcinoma
2. Intracystic carcinoma
3. Spindle-cell carcinoma, "adenosarcoma"
4. Adenoid cystic carcinoma
5. Carcinoma with osseous and cartilaginous metaplasia
6. Squamous carcinoma
7. Malignant variant of fibroadenoma and cystosarcoma phyllodes

### PAGET'S DISEASE OF THE NIPPLE

Paget's disease has long been recognized as a clinical and pathologic entity and as such does not require discussion. The lingering debate as to whether this is a disease primary in the epidermis of the nipple or whether it represents an outward extension of cancer cells from underlying mammary ducts cannot be settled here. Certainly in the ordinary case of Paget's disease of the nipple there is easily identifiable underlying carcinoma of mammary ducts (Figs. 1 and 2) having no structural peculiarities that would separate it from those duct carcinomas that are not accompanied by Paget's disease. Certainly there are those cases, the exceptional ones, where underlying involvement of mammary ducts is distinctly minimal, but we have never had an example where we could say that the underlying mammary ducts were free from involvement. To sustain fully the thesis of primary origin in the epidermis a case is needed in which the entire nipple was sectioned serially and shown to have mammary ducts entirely free from malignant alteration. From time to time random sections have been seen in which the process was limited to the epidermis. Invariably when further material from such a case was cut, involvement of underlying ducts was shown. If Paget's disease is primary in the epidermis it seems rather odd that the infiltrating tumor associated with Paget's disease of the nipple is always a tumor with the morphologic characteristics of carcinoma of the breast and that this structure is present in metastases. If Paget's disease of the nipple is primarily epidermal in origin, it is peculiar that the infiltrating tumor does not commonly assume the form of an epidermoid carcinoma in both the primary tumor and its metastases. Failure to do this puts considerable strain on the theory of origin in epidermis. Even when a lesion identifiable as Paget's disease of the nipple shows epidermoid structural traits, this is not proof of primary epidermal derivation since duct carcinomas of the breast may assume the properties of epidermoid carcinoma in both the primary tumor and node metastases in the absence of overlying Paget's disease of the nipple. To cite examples of extramammary Paget's disease does not necessarily solve the problem of this disease of the nipple. The impression has been gained that some cases of extramammary Paget's disease are not critically diagnosed. Where



the resemblance to Paget's disease of the nipple is satisfactory, it is necessary that evidence be presented that sweat gland ducts in the region were not involved. Extramammary Paget's disease is so uncommon that all of its histogenetic problems have not been settled. We have seen no case which showed critically the primary origin of Paget's disease in the epidermis of the nipple.

Fig. 1.



Fig. 2.

Fig. 1—Paget's disease of the nipple; involv  
Fig. 2—Paget's disease of the nipple; involv

The clinical implications of Paget's disease of the nipple are, for the vast majority of cases, quite clear-cut and they indicate the necessity for radical amputation of the breast. Even in Paget's disease of the nipple, in which there is no clinically palpable underlying lesion, one undertakes considerable responsibility when recommending any procedure short of radical mastectomy. Metastases have been found in Paget's disease when no definitive tumor was palpable. Sections from such cases have shown the presence of miniature infiltrating carcinoma.

#### CARCINOMA OF MAMMARY DUCTS

##### *Noninfiltrating Tumors.—*

*Papillary carcinoma:* The term noninfiltrative papillary carcinoma designates a tumor of specific histologic type in a phase highly favorable for cure by means less radical than those required for infiltrating carcinomas. Structurally the disease is limited to the mammary duct system and either the large, medium-sized, or small radicles may be affected. Whereas there may be extensive spread throughout a large portion of the duct system, there is usually fairly well-defined segmental distribution having at least quadrant localization. In some cases one gets a distinct impression of multiple foci of origin and in the rare case there are apparently independent primary sources in different quadrants of the breast. Microscopically the tumor is characterized by atypical papillary hyperplasia of duct epithelium which is heaped up in solitary finger-like projections which usually do not possess a vascularized stalk (Fig. 3). Papillary anastomosing strands of tumor bridge the lumen of the duct leaving vacant spaces which result in a cartwheel-like structural pattern. In some areas the cell proliferation becomes so dense that basic papillary properties are overgrown. The duct lumen is progressively reduced and finally obliterated. Characteristically, the central areas of intraductal tumor do not undergo necrosis as is the case in comedocarcinoma. Some of these tumors do not exhibit a high degree of cellular atyp. The individual cells are usually of medium size and do not vary a great deal in configuration and stainability. Hyperchromatism is not impressive and the rate of cell division is low. The histologic alteration of greatest significance is a disturbance in cell polarity. These various factors combine in quality and degree beyond that found in benign duct papillomatosis. It must be acknowledged that there is a zone of altered cell growth where the diagnosis of carcinoma versus atypical papillomatosis is a question of occult distinction and must be accepted or rejected on grounds of faith in the pathologist or lack of it. In some instances in which the presence of noninfiltrating papillary carcinoma is quite obvious, there will be additional outlying or adjacent foci in which the degree of structural change is distinctly less advanced and this leads one to believe that pre-existing papillomatosis had been present and had undergone malignant transformation.

In our material this is a rare variety of mammary carcinoma seen only two to three times per year, during which time about 500 surgical specimens of mammary carcinoma are examined in the laboratory. As a result of having seen a large number of referred patients in whom the diagnosis of noninfiltrating

papillary carcinoma has been made, we are convinced that it is made much too often. The vast majority of such referred diagnoses proved to be nothing more than benign duct papillomatosis. The error in diagnosis is hence most often made in the direction of unjustified diagnosis of carcinoma.

A preoperative, clinical diagnosis of carcinoma in these patients is unlikely since the secondary physical signs of breast carcinoma are not present

FIG. 3

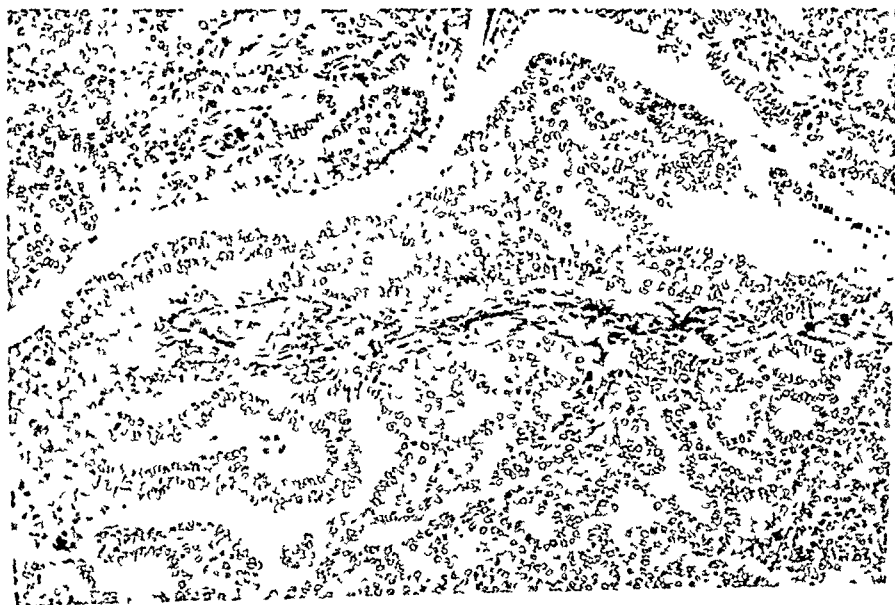


FIG. 4

Fig 3—Noninfiltrating papillary carcinoma of ducts  
Fig 4—Infiltrating papillary carcinoma

and the lesion is not often well demarcated and discrete. Bleeding nipple may or may not be present. For these reasons such cases are apt to come to the pathologist's attention at the time of operation when a locally excised portion of breast tissue is submitted for frozen section. In the gross, one sees multiple mammary ducts which appear partly or entirely filled with friable grayish-white tissue. The central, intraductal necroses of comedocarcinoma are not present. It is very difficult in some cases to be certain from frozen sections that there is no infiltration. Under these circumstances it is our policy to recommend simple mastectomy. If no infiltration is found after study of subsequent paraffin sections, further operative procedure is unnecessary. If, however, the tumor is shown to be infiltrating, it is obligatory that radical dissection be carried out. In no case of noninfiltrating papillary carcinoma is it safe to stop short of simple mastectomy since no one can guess accurately the distribution of the tumor within the breast.

*Comedocarcinoma:* The noninfiltrating form of comedocarcinoma differs from papillary carcinoma in that the growth within the ducts is generally more solid and is accompanied by central necrosis. On gross examination there is an expressible core of soft or semisolid, usually somewhat greasy, material. It is this property of simulating a comedone that is responsible for the descriptive term employed. Comedocarcinomas may arise in any portion of the duct system. If one plots the distribution of these tumors he will discover that, contrary to usual teaching, they more frequently begin in the smaller and intermediate duct divisions. The intraductal proliferation of cells often expands a small duct to and beyond the dimensions of the major mammary ducts. True enough the most classical and impressive cases do involve the larger channels but at the same time they are exceptional. Histologically the intraductal proliferation is decidedly atypical in a degree far exceeding that which is usual in papillary carcinoma. The cells concerned are usually larger, are more hyperchromatic, show greater loss of polarity, and in an overall sense are much more anaplastic (Fig. 5). In so far as the pathologist is concerned, these tumors present in part the same frozen section problem as noninfiltrating papillary carcinoma. They are not so difficult, however, from either the gross or the microscopic point of view.

A true noninfiltrating comedocarcinoma is another rare type of mammary cancer constituting less than 1 per cent of all cases. The chief reason for specific mention of this tumor as an anatomic type is that it represents another example of breast carcinoma rationally treated by means of simple mastectomy.

#### *Infiltrating Tumors.—*

*Infiltrating papillary carcinoma:* Infiltrating papillary carcinoma of mammary ducts represents a later phase of the tumor described under papillary carcinoma. In the more advanced invasive stage, its papillary qualities are well maintained (Fig. 4). The tumor incites little or no reactive fibrosis in the breast and on section it appears cellular, soft, and friable. Considerable bulk is commonly attained and other attributes are circumscription without encapsulation and a tendency to irregular necrosis which is usually central. Skin attachment

is customarily very late in the course of the disease and seldom seen unless the tumor is very large. Rate of growth is slow and when there has been a history of recent rapid enlargement, this can nearly always be explained by finding large areas of anemic or hemorrhagic necrosis with edema and exudative reaction in and about the tumor. Important to mention is the ordinarily long de-

Fig. 5.

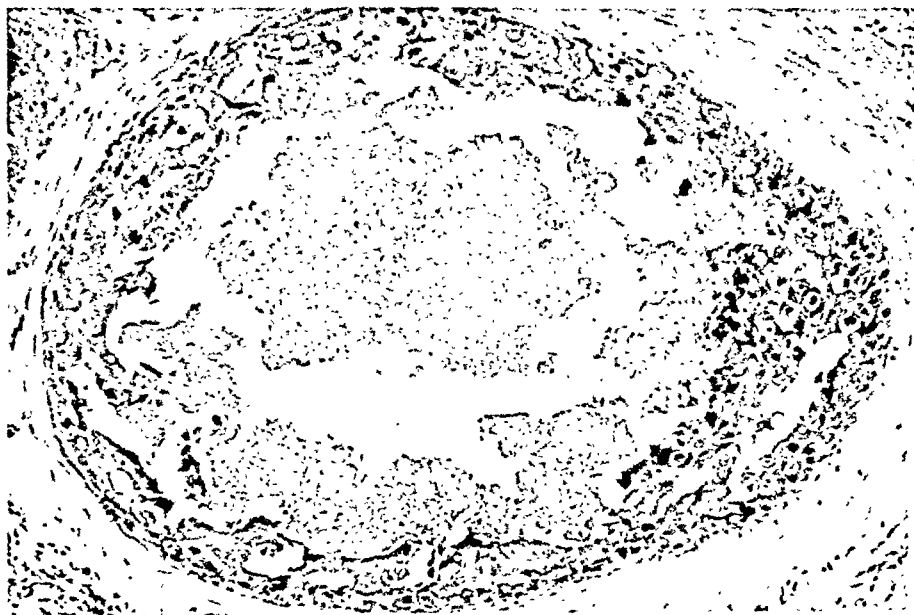


Fig. 6.

Fig. 5.—Noninfiltrating comedocarcinoma.

Fig. 6.—Infiltrating comedocarcinoma.

lay before axillary node involvement takes place. In the breast tissue itself the tumor shows little ability for intramammary spread along periductal or other lymphatic channels.

Due to aforementioned low-grade infiltrative qualities, these tumors are easily movable on palpation of the breast. This factor, combined with a lack of firmness, has in a number of instances led to a clinical diagnosis of fibroadenoma. The practice of aspiration biopsy at Memorial Hospital obviates any delay in correct diagnosis. In those cases in which local excision is done the gross aspect or, if needed, frozen section will disclose the true nature of the tumor and the radical operation can then be carried out. Conservatism is unwarranted in spite of the better prognostic outlook.

*Infiltrating comedocarcinoma:* Comedocarcinoma is almost invariably infiltrative when its presence is discovered. The only feature distinguishing it from other forms of infiltrating duct carcinoma is the accented feature of intraductal growth (Fig. 6) which is manifest both grossly and microscopically. If the disease is very advanced little of the quality of intraductal growth is retained and, as a consequence, such tumors lack much of the distinctiveness of classical comedocarcinomas. There is every range of balance between the properties of intraductal growth and those of infiltration. Naturally where infiltration is minimal the prognosis is correspondingly more favorable.

The histologic characters of infiltrating comedocarcinoma are very varied and from case to case one encounters tumors that grow after the fashion of ordinary scirrhous carcinoma or medullary carcinoma, or perhaps the tumor becomes largely colloid. Occasionally the cytology corresponds to that of so-called apocrine sweat gland carcinoma and again certain areas of an infiltrating comedocarcinoma become spindle cell or otherwise pleomorphic in make-up. In other words the infiltrating forms of comedocarcinoma have all the histologic potentialities of the various forms of duct carcinoma next to be described.

*Infiltrating duct carcinoma with productive fibrosis:* Tumors comprising the group of carcinomas with productive fibrosis are far and away the commonest forms of mammary cancer, aggregating roughly 70 per cent. Included here are the tumors that may be summed up as "ordinary mammary scirrhous." We are broadening this interpretation, however, to include some more cellular varieties in which the growth is less scirrhous. Even those cellular tumors referred to as carcinoma simplex show more or less desmoplasia or productive fibrosis, and to include in a classification scheme a separate heading for every microscopic variant creates added complication—an end already rather capably achieved in the foregoing classification.

For extreme forms of scirrhous carcinoma the term fibrocarcinoma has sometimes been used. For the more cellular form of this type one may employ the descriptive term carcinoma simplex. As would be expected, the majority of tumors falling in this large group lie between these extremes. Correspondingly, the degree of structural distortion seen in the histologic growth patterns is widely variable. Certain members of this group are quite orderly and grow

is customarily very late in the course of the disease and seldom seen unless the tumor is very large. Rate of growth is slow and when there has been a history of recent rapid enlargement, this can nearly always be explained by finding large areas of anemic or hemorrhagic necrosis with edema and exudative reaction in and about the tumor. Important to mention is the ordinarily long de-

Fig 5

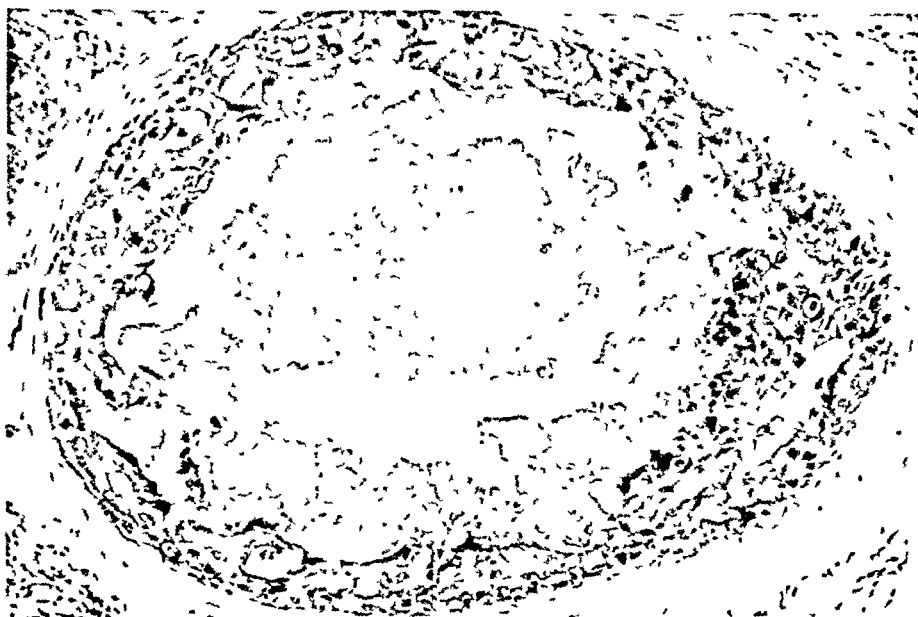


Fig. 6

Fig 5—Noninfiltrating comedocarcinoma  
Fig 6—Infiltrating comedocarcinoma

examples of almost acellular tumors in which the cells are so sparse that diagnosis of cancer in a limited field might be difficult. In such highly fibrotic tumors the infiltrating epithelial cells are sometimes so densely compressed between collagen fibers that they become narrow and spindle in contour in such a way that they simulate connective tissue cells.

FIG. 9.



FIG 10.

Fig 9.—Infiltrating duct carcinoma with productive fibrosis  
 Fig 10.—Infiltrating duct carcinoma with productive fibrosis



The macroscopic characteristics of these tumors are easily recognized and these are the forms of mammary carcinoma usually described when the classical gross traits of mammary carcinoma are enumerated. The majority of these tumors are not rounded but are discoid and have distinctly irregular edges which radiate from the general periphery of the tumor into adjacent fibrous or fatty breast tissue. An outstanding attribute is firm and almost unyielding induration. Under the knife they cut with increased resistance and the exposed surface is depressed below the level of the surrounding breast tissue. The cut surface of the tumor exhibits the prosaic yet authentic striate, yellowish, chalky streaks, scattered over a generally grayish or pale grayish-yellow background. Spontaneous hemorrhage and large areas of necrosis are much less common in this type of mammary carcinoma than in many others. On the average these tumors are 2 to 3 cm. in greatest diameter. Great bulk is somewhat exceptional.

Radical mastectomy is the only approved surgical procedure for tumors in this infiltrating group. This applies even to those tumors that are designated numerically as of low-grade malignancy. Whereas the frequency with which the axilla is involved in these tumors of lower grade of malignancy is distinctly less than the more histologically malignant, it is too frequent to justify the risk of limited breast surgery.

*Medullary carcinoma:* Medullary carcinoma is characteristically composed of large, oval, rounded or polygonal cells with abundant basophilic cytoplasm and large vesicular nuclei. The cells are put together usually in rather broad, anastomosing, medullary or plexiform masses. In some of the tumors there is fairly well-developed papillary quality and in such areas the formation of lumina is not unexpected. In still other examples the growth pattern is highly indifferent and almost syncytial in its diffuseness. The degree of hyperchromatism, nuclear variation, and cytoplasmic variation as to size and shape is not great. Hemorrhagic or anemic necrosis is common. The tumors are apt to be quite rich in mitoses.

A great many medullary carcinomas are accompanied by abundant infiltrations of small lymphocytes to such an extent that they seem to be a formal component (Fig. 11) in the make-up of the tumor. Their presence cannot be explained as a reaction to broken down tumor since they may be seen in very small tumors that do not have foci of necrosis. They arouse the speculation that they are a manifestation of host reaction to the presence of tumor. This structural peculiarity is sufficient to justify specific recognition and to report such tumors as medullary carcinoma with lymphoid infiltrate.

Grossly, medullary carcinomas have highly distinguishing qualities and they stand in contrast to the group described in the preceding section. They are commonly quite bulky, measuring 4, 5 and 6 cm. in diameter, and now and then these dimensions are doubled. They are rounded or globoid, cut with little resistance, and although not encapsulated these tumors are distinctly circumscribed and present a smooth periphery. On cut section the exposed surface bulges above the level of the surrounding tissue, the tumor is soft, and chalky streaks are unexpected. Where the cancer is fully viable it is grayish-white,

but as a group these tumors are quite prone to spontaneous hemorrhage and necrosis and for this reason may present variegated coloring. Size for size they are distinctly less infiltrating than scirrhus carcinomas as judged by the local infiltration in the breast as well as the frequency of axillary node metastases. Due to relatively low-grade infiltrative tendencies and the habit of circumscription, they are apt to show clinically little or no skin attachment or dimpling.

Fig. 11.

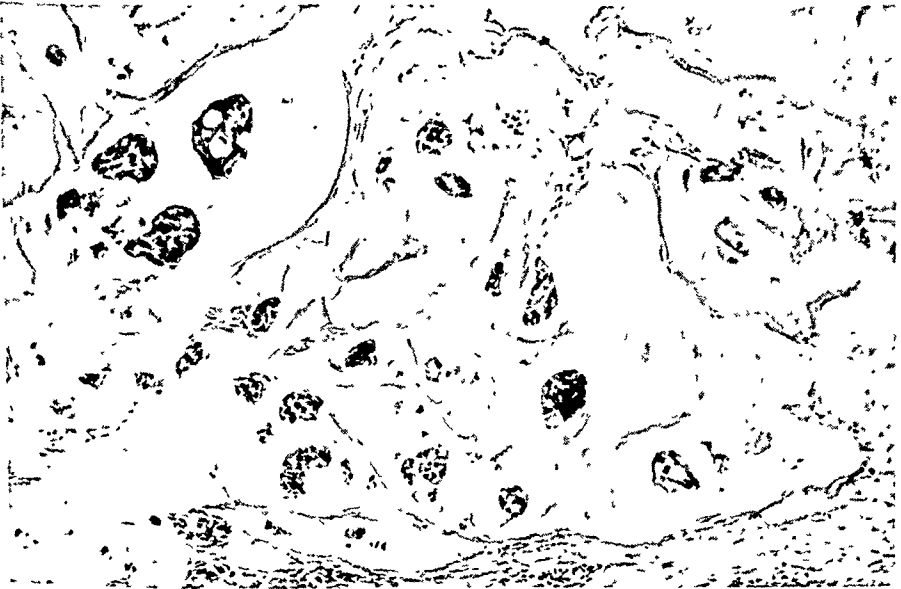


Fig. 12.

Fig. 11.—Medullary carcinoma with lymphoid infiltrate.

Fig. 12.—Colloid carcinoma of breast.

As a rule the axillary nodes do not contain tumor unless the primary is as large as 1.5 to 2 cm. and tumors may reach very large size or even fungate without having metastasized to the axilla. They constitute about 15 to 20 per cent of breast carcinomas.

In surgical control of this disease, radical mastectomy is again the only procedure that can be properly advised. Even though these tumors have seldom produced axillary metastases when  $1\frac{1}{2}$  cm. or smaller in diameter, this does not constitute any assurance for a particular case and any conservative procedure involves increased risk to the patient.

*Colloid carcinoma:* The diagnosis of colloid carcinoma of the breast is necessarily imperfect in many cases, inasmuch as it represents the employment of a descriptive term for a histologic alteration which is present from case to case in varying degrees of completeness (Fig. 12). When to use the term and when not to use it is a more or less arbitrary matter which will differ from person to person. Where a laboratory is handling a bulky material there is apt to be little inclination to employ this term unless the gelatinous character of the tumor is highly developed. On the other hand, if a limited amount of pathologic material from breasts is available this term is likely to be much more readily applied because of the natural human instinct to dress up material as gaily as possible. Particularly in some rather bulky mammary cancers there is a tendency toward colloid change. On the other hand, a carcinoma of the breast is occasionally encountered as small as 1 cm. or less in size in which the whole body of the tumor is soft and gelatinous with no firm noncolloid portion. Our own practice is to employ the term colloid carcinoma when this is an obvious character seen in the gross. When the colloid aspect of the tumor is a random microscopic finding, we are inclined to designate the tumor as an infiltrating duct carcinoma, partly colloid.

We have not as yet noted colloid change in a tumor which had characteristics indicating origin from mammary lobules. This is not necessarily a permanent point of view since it is hardly possible to predict in any group of malignant epithelial tumors the inability to show colloid change.

Sometimes one is hard put to designate the degree of malignancy in a colloid carcinoma. This is principally true in those tumors in which the cancer cells are very sparse. All that can be done is to base the idea of the malignancy of the tumor on what can be seen but it is not a good plan to take one's ideas of the grading of a colloid carcinoma too seriously. Some of those tumors which are both small in dimension and relatively acellular will be found to have produced axillary metastases, and it is unwise to trifle with colloid carcinoma no matter how sluggish it appears under the microscope. Grading in most colloid carcinomas can best be based on the structure of noncolloid portions.

#### CARCINOMAS OF MAMMARY LOBULES

*Noninfiltrating Lobular Carcinoma.*—In a previous publication<sup>2</sup> we referred to noninfiltrating lobular carcinoma as "lobular mammary carcinoma in situ." This form of mammary carcinoma usually goes unrecognized. In all probability

this is largely caused by its extremely low rate of occurrence. Perhaps, because of lack of material or interest in the structural attributes of mammary lobules, pathologists have spent little effort in their study. Evidence in this direction is furnished in the recently published cumulative index of the *American Journal of Pathology* covering a twenty-year period from 1925 through 1944. Included are only twelve articles on human breast pathology and but one of these is primarily concerned with the mammary lobules.

Microscopically, one finds in limited and sometimes large areas numbers of mammary lobules, some of which are decidedly larger than normal and whose cellular make-up is greatly changed (Fig. 13). The cells within the acinar components, although not large, exceed the size of normal acinar cells. They pile up in a loose or compact fashion with no orderly layering. Almost always the acinar lumina are obliterated and the cells within lack coherent arrangement. They differ little in size but assume various shapes tending to be round or ovoid where there is least cell crowding. The nuclei are not hyperchromatic and may actually appear pale, somewhat after the manner of the cells in Paget's disease of the nipple. Mitoses are few. The cytoplasm is moderately opaque and does not have outspoken eosinophilic or basophilic quality. The involvement of a single lobule may be complete or partial, and in the latter instance nice contrast is demonstrated. In making the diagnosis microscopically of lobular carcinoma in situ, one must not confuse the intralobular extensions of tumors which are of duct origin. Such extensions are only superficially confusing with true lobular carcinoma in situ.

Lobular mammary carcinoma in situ cannot be diagnosed clinically nor can a diagnosis be made on gross pathologic examination. All that one sees in the gross are groups of rather large lobules which may be more or less closely spaced and concentrated within a relatively limited area. For this reason, this form of noninfiltrating carcinoma represents an incidental finding in local excisions which have been done for presumably benign conditions. The only physical sign elicited where this lesion exists is ill-defined induration and this only in the exceptionally well-developed case. In our opinion, simple mastectomy should be done when the diagnosis of lobular carcinoma in situ is made and if, in subsequent pathologic material, infiltration is discovered, further surgical procedure is necessary.

*Infiltrating lobular carcinoma:* Infiltrating lobular tumors make up about 3 to 5 per cent of all breast carcinomas. As a histologic entity they are not widely recognized. The microscopic structural pattern assumed by these tumors is, however, quite characteristic once its peculiarities are appreciated. To be certain of the identity of this infiltrating form of cancer as one arising in lobules requires the observation of a large mass of breast material sufficient to supply enough key cases which show transitions from the noninfiltrating form of the disease to the fully infiltrating tumor. The infiltrating portions of lobular carcinomas typically reveal threadlike strands of tumor cells rather loosely dispersed throughout a fibrous matrix. After infiltration has occurred there is

no tendency for the cells to simulate atypical lobules. Sheetlike growth is distinctly uncharacteristic. The individual cells are small or medium-sized and commonly elliptical or spindle-shaped due to the denseness of the surrounding fibrous tissue matrix (Figs. 15 and 16). They are rather uniform in their staining properties and exhibit relatively little cytologic irregularity. The structure of the tumor in metastases is apt to contrast considerably with the

Fig. 13.

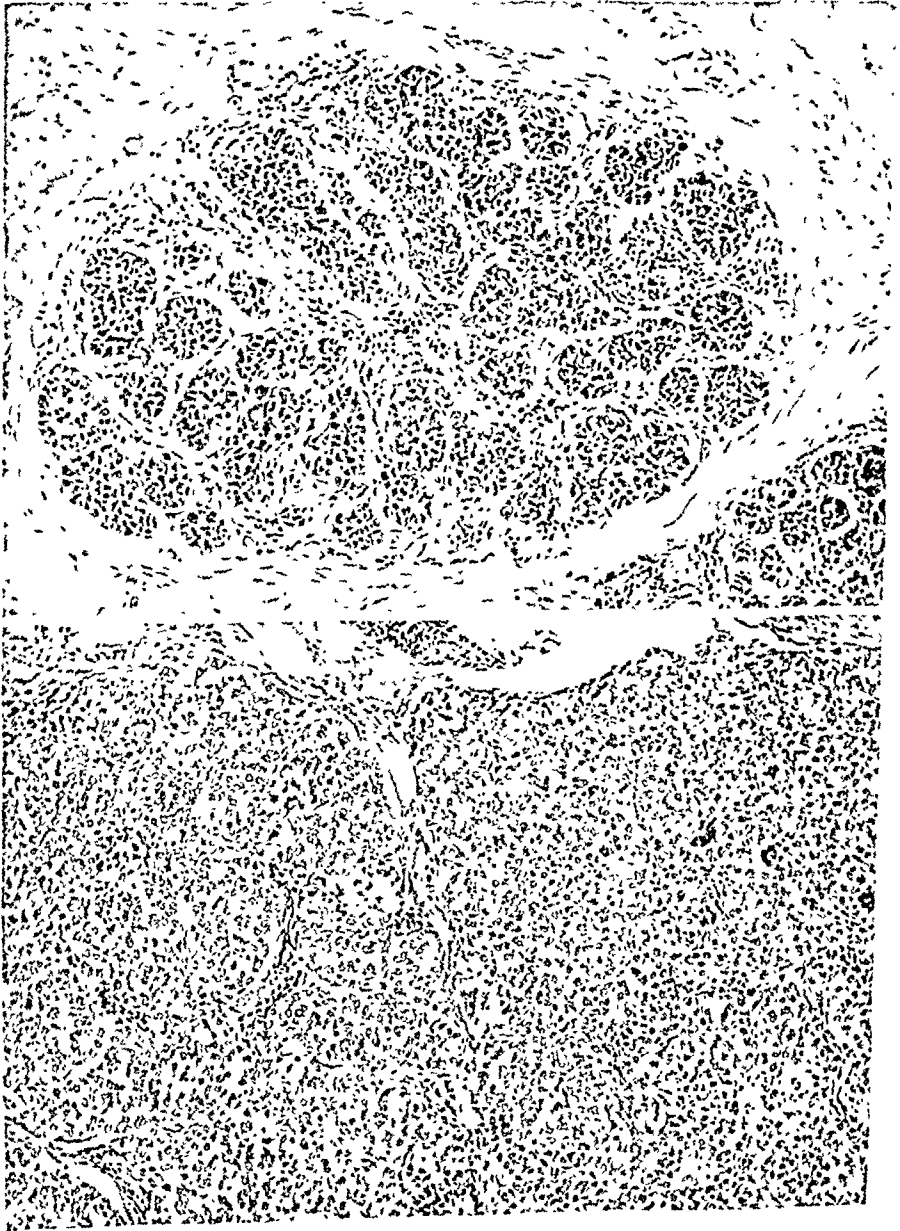


Fig. 14.

Fig. 13.—Noninfiltrating lobular carcinoma (lobular carcinoma in situ).  
Fig. 14.—Early infiltrative phase of lobular carcinoma.

commonly rather acellular structure of the primary tumor. In extreme examples the axillary metastases actually simulate lymphosarcoma. We have seen several referred patients in whom the pathologic diagnosis of lymphosarcoma had been made from sections of axillary nodes which contained metastases from undiscovered breast primaries. Great cellularity in the primary tumor is unusual but there are occasional cases in which this does occur.

Fig. 15.

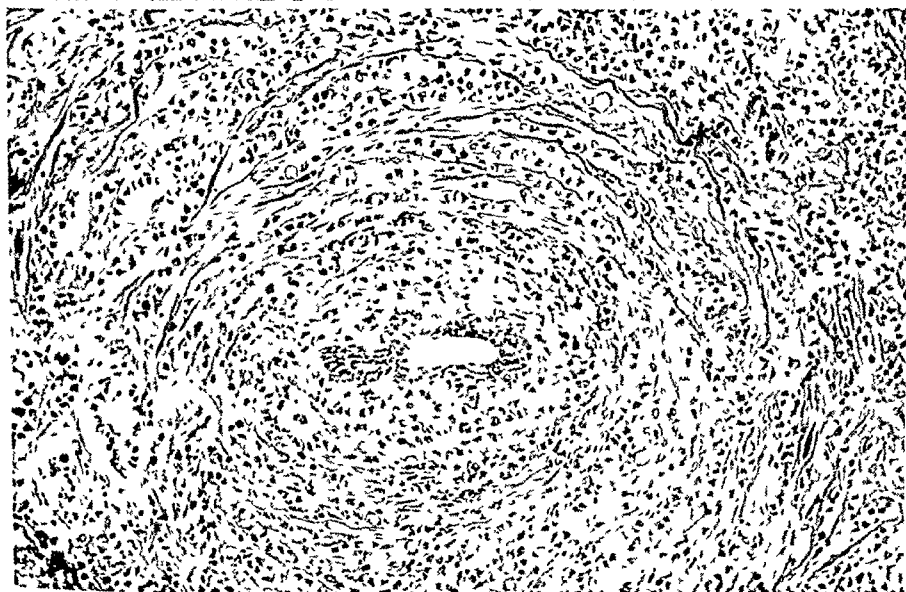


Fig. 16.

Fig. 15.—Noninfiltrating and infiltrating lobular carcinoma

Fig. 16.—Periductal infiltration pattern likely to be assumed by lobular carcinoma

In the gross, infiltrating lobular carcinomas are more apt to resemble scirrhus carcinomas than other gross anatomic types. The tumors, as a rule, are discoid or somewhat irregular in shape and rather poorly demarcated. They are tough and firm and are less apt to show chalky streaks so common in ordinary mammary scirrhus. On some occasions the gross specimen can be quite confusing and misleading. These episodes usually come about at the time of operation when a locally excised specimen of breast tissue is sent in for frozen section diagnosis. Such a specimen may present no distinctly visible lesion and yet contain a palpable area of peculiar induration, the precise limits of which are vague. Such lesions can cause difficulty in frozen section diagnosis, since the cell proliferations are in minute or single-cell strands or composed of isolated single-cell units. After the diagnosis of cancer is made it is well to be prepared for querulousness from the operating surgeon who understandably would like to be operating for something more finite than indistinct induration.

These tumors are fully aggressive mammary cancers and as such call for radical surgical measures.

#### RELATIVELY RARE CARCINOMAS

*So-called Sweat Gland Carcinoma.*—It should be understood here that sweat gland carcinoma is not carcinoma of the sweat gland appendages of the skin of the breast. The term sweat gland carcinoma needs further qualification and is more properly referred to as apocrine sweat gland carcinoma since the cell type concerned has real resemblance to the cells of cutaneous apocrine sweat glands. These tumors constitute about 1 per cent of mammary carcinomas and are a specific histologic type characterized by large eosinophilic cells which are oftentimes columnar and contain abundant eosinophilic cytoplasm and relatively small nuclei (Fig. 17). All of these qualities, with the exception of the eosinophilic quality of the cytoplasm, are subject to considerable variation. In tumors where this characteristic does not exist the diagnosis is not justified.

In the classification given, so-called sweat gland carcinoma has not been listed under a specific anatomic site of origin such as duct or lobule. Avoiding this was purposeful. The cells making up these tumors bear considerable resemblance to cells found in both the ducts and lobules of the breast which have undergone apocrine metaplasia. In the material that we have available which gave evidence for a site of origin, the mammary ducts were implicated. In the unusual but most satisfactory case, highly convincing transitions are seen ranging from typical apocrine epithelium to apocrine epithelium in atypical hyperplasia to intraductal apocrine sweat gland carcinoma and finally to infiltrating carcinoma made up of apocrine-like cells. Since, however, apocrine metaplasia commonly affects the lobular epithelium, it does not seem justifiable to exclude the lobules as a potential source of origin.

There are no unique characters that make it possible to identify these tumors grossly. Customarily they resemble the more cellular infiltrating duct carcinomas with more or less productive fibrosis. Extreme degrees of fibrosis are not usual. Occasionally the gross appearance is that of a comedocarcinoma.

The morphologic specificity of these tumors is evident only microscopically. The therapeutic implications of infiltrating mammary carcinomas apply here. If perchance a noninfiltrating form is encountered, simple mastectomy should suffice.

*Intracystic Carcinoma.*—It is distinctly infrequent to see an unequivocal anatomic example of this type of mammary carcinoma. That this should be a

Fig. 17.

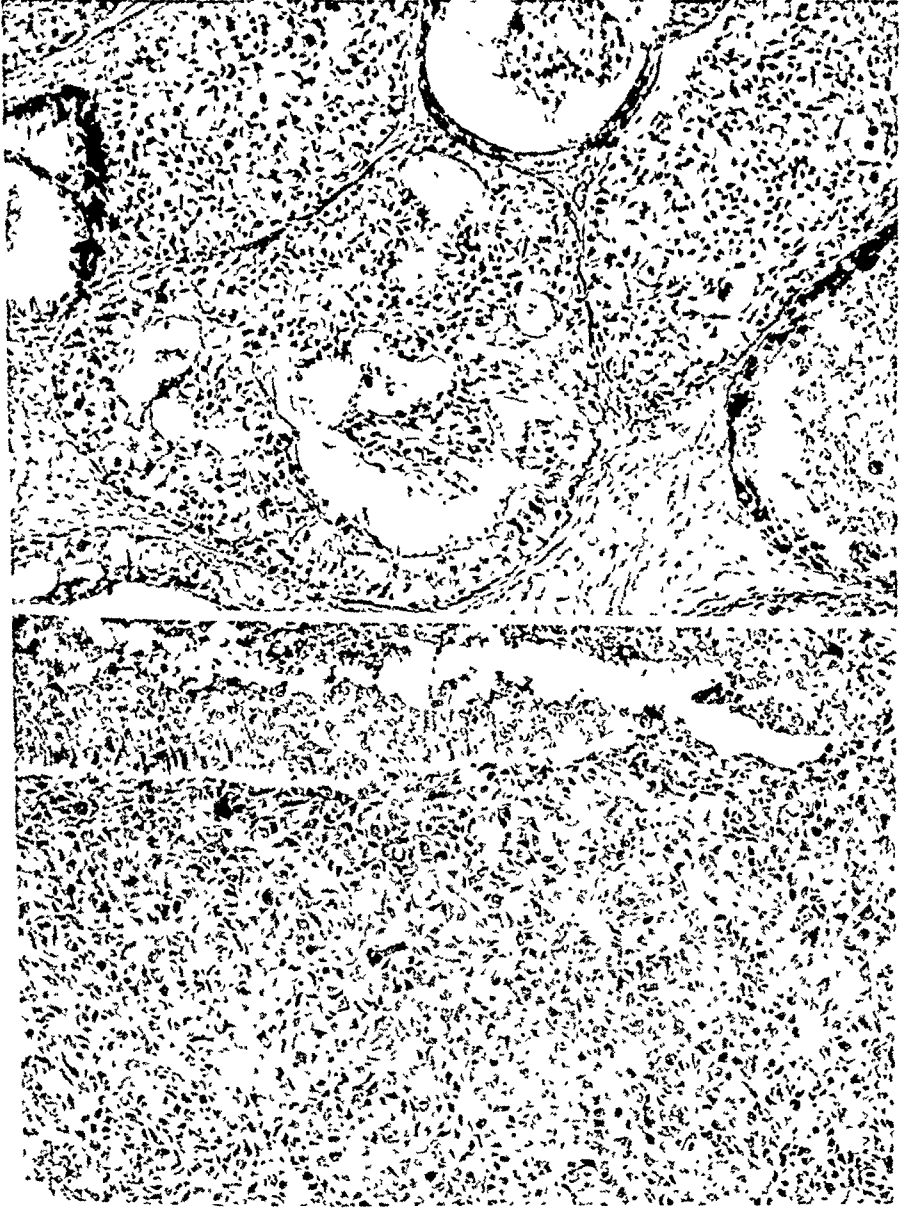


Fig. 18.

Fig. 17.—So-called apocrine sweat gland carcinoma of breast.

Fig. 18.—Duct carcinoma with spindle and polyhedral cells



rare form is not surprising, inasmuch as the vast majority of cysts in the breast lose their epithelial lining when they become a few millimeters or more in diameter. Even in those cysts of the breast which still retain epithelial lining, atypical hyperplastic epithelial changes are nearly nonexistent. Intracystic papillomas are themselves very few in number if one includes only authentic examples of this lesion and excludes the common intraductal papilloma. The latter lesion is oftentimes loosely referred to as an intracystic papilloma, which it, indeed, is not. Sometimes in a true intracystic carcinoma there is residual noncancerous papilloma but these traceable lesions are almost a curiosity. This anatomic type has purposely been excluded from listing under either the tumors of duct or lobule origin since by the time that an intracystic carcinoma has developed, its exact point of origin is no longer demonstrable. It is difficult enough to decide where 1 and 2 mm. sized cysts arose. This tumor is more distinctly a gross than a microscopic entity.

In this numerically small group of mammary tumors, now and then a non-infiltrating tumor is discovered confined to the wall of the cyst. Usually infiltration is present and it is more apt to be advanced than limited. Even where there is considerable bulk of solid infiltrating tumor, at least a portion of the cyst is uninvolved in the malignant process. The intracystic portions of the tumor are nearly always partly papillary but they may be almost entirely solid and very cellular. The infiltrating portions assume a wide variety of structural patterns varying from highly cellular tumors to those that are predominantly scirrhous in character. We have never seen an infiltrating intracystic carcinoma which assumed any growth trait not common to one of the several forms of definitely established duct carcinoma. In no case has the intracystic carcinoma partaken of the histologic qualities seen in lobular carcinoma.

The disease is a rare one and hence opportunities to employ different forms of surgical procedure will be correspondingly few. In the rare case where one can be convinced of lack of infiltration, simple mastectomy as opposed to radical mastectomy is the reasonable form of treatment, but with infiltration there are all the implications of cancer of the breast in the ordinary sense.

*Spindle-cell Carcinoma, "Adenosarcoma."*—To the preceding terms carcinosarcoma may be added. Usage of these terms is not uniform. It is our practice to use such terms as adenosarcoma and carcinosarcoma as little as possible. They can of course be used in either a descriptive or a derivative sense. In the first instance, one would signify a malignant epithelial tumor having areas which simulate a malignant connective tissue tumor. When used in a derivative sense, that is, a histogenetic sense, the terms indicate a malignant tumor containing cells of both epithelial and mesodermal origin. In so far as the breast is concerned, it appears probable that the only tumor properly meriting a diagnosis of adenosarcoma or carcinosarcoma is the malignant variant of cystosarcoma phyllodes or fibroadenoma in which there is malignant change involving both epithelial and connective tissue cells. No definite rules have been established as to the usage of such terms and when one employs them in manu-

script, explanation of usage is imperative to avoid confusion. In this classification these terms are used in a purely descriptive sense.

Spindle-cell carcinoma of the breast is so uncommon that only once in several hundred cases is it necessary to make the diagnosis. Thus the problem of terminology is a trifling one. Whether or not one is justified ever in making a diagnosis of spindle-cell carcinoma, unless there is at least some traceable gland forming or other epithelial quality, is a debatable matter among pathologists. Here again one deals in attitudes and is hard put to defend satisfactorily that attitude which has been assumed. A doctor is apt to be friendly or unfriendly toward the diagnosis of spindle-cell carcinoma in about that degree to which he accedes to the metaplastic capabilities of neoplasia in general and it is also dependent upon how broad a mass of neoplastic disease he has had to study. In making the diagnosis of spindle-cell carcinoma in the absence of definitely demonstrable epithelial structure, it is perhaps preferable to acknowledge some doubt as to the ultimate accuracy of the diagnosis. In this way one can avoid a certain amount of unnecessary argument and yet maintain his private opinion. Painstaking study of multiple blocks will oftentimes turn up the desired indisputable epithelial areas. It is also noteworthy that these tumors metastasize to regional lymph nodes, which is not the expected behavior in sarcoma. As a general rule applicable to neoplasms as a whole, it may be stated that it is much more common for an epithelial tumor to show pseudosarcomatous areas than it is for a connective tissue tumor to show pseudoepithelial areas. We have spoken of spindle-cell carcinoma in this section but it must be added that some of those tumors which are predominantly spindle cell show, in addition to this type of cell, a great variety of cells of all sizes and shapes which grow in a more or less indiscriminate pattern (Fig. 18).

These pleomorphic mammary tumors which have epithelial and pseudosarcomatous properties are quite apt to be bulky. Other factors associated with them are long duration and secondary ulceration of overlying skin. In an occasional case in which there are biopsies from succeeding local recurrences, it is sometimes observed that the recurrences at one time partake largely of epithelial quality, while at other times the pseudosarcomatous pattern is predominant. To our minds these observations reinforce the fundamental view that the tumors are primarily epithelial in origin. An exception has already been cited.

*Adenoid Cystic Carcinoma.*—This is a vanishingly rare breast carcinoma. Structurally it is absolutely indistinguishable (Fig. 19) from the adenoid cystic carcinoma of major and minor salivary glands as well as from mucous glands of trachea and bronchi. The same histologic type of tumor is also seen very occasionally arising from cutaneous sweat glands. We have seen only three examples of this tumor primary in breast. In one of these the adenoid cystic areas blended with areas growing like ordinary duct carcinoma with productive fibrosis. In addition there were ducts showing atypical papillomatosis and intraductal carcinoma. These findings suggest that the adenoid cystic carcinoma is another histologic variety of duct cancer.

The available inventory of these tumors is so small that a comprehensive account of their clinical behavior is not available. In other locations they are well known to have the ability to metastasize even though the clinical course may be prolonged. Until evidence to the contrary is presented, radical operation should be carried out.

Fig. 19

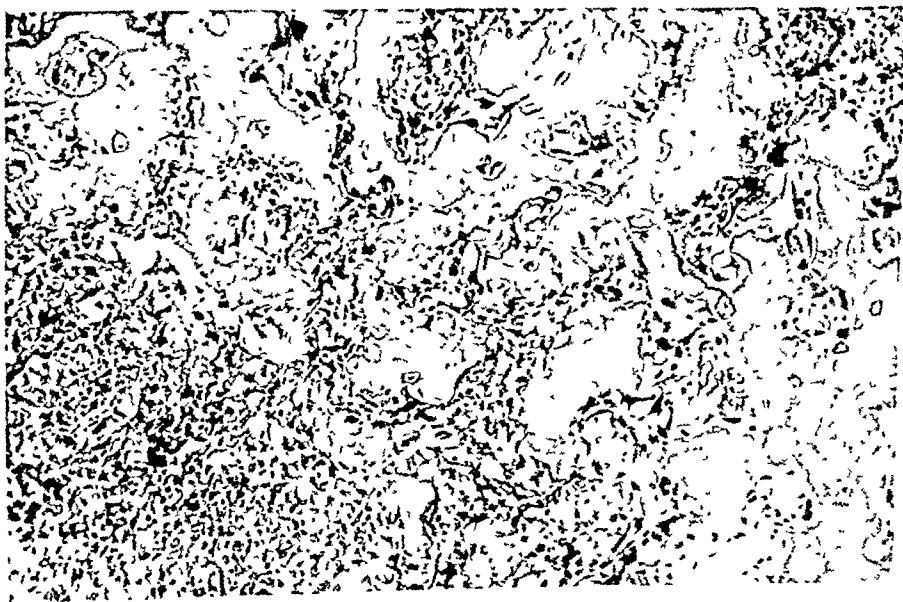


Fig. 20.

Fig. 19.—Adenoid cystic carcinoma of breast  
Fig. 20.—Mammary carcinoma with osseous metaplasia

*Mammary Carcinoma With Osseous and Cartilaginous Metaplasia.*—This rare group of mammary carcinomas furnishes some of the most structurally bizarre breast tumors. The aforementioned metaplastic characters may be seen in only very limited areas of a tumor growing as infiltrating duct carcinoma or they may dominate the histologic picture almost to the exclusion of other elements. Not a few of these tumors show areas growing as squamous carcinoma. Invariably there is more or less spindle-cell component which can in most cases be traced in transitional stages to malignant epithelial cells. Actually it seems that spindle-cell metaplasia is an intermediate stage preliminary to the assumption of the osseous and cartilaginous qualities (Figs. 20 and 21). In some cases the cartilaginous areas predominate over the osseous and sometimes the reverse is true. Transition zones are not difficult to find. Although calcific bone trabeculae do occur, it is more common that the "osseous" component resembles osteoid tissue. Cytologically the osseous and cartilaginous areas appear malignant. This is apt to prompt the diagnosis of osteogenic sarcoma of the breast. We do not deny the possible existence of a mesodermal tumor of the breast having a structure consistent with osteogenic sarcoma since soft part sarcomas having these characters are well known to exist in other locations. It is felt, however, that the vast majority of breast cancers with such structure are examples of extraordinary metaplasia in fundamentally epithelial tumors. If, in a given case, no traceable transitions from epithelium can be detected, this thesis cannot be supported in a convincing manner. Having seen a considerable number of cases in this category, the impression has been gained that pathologists are so struck by the exotic aspect presented that no great search for histogenetic phases is made. It is a bit more sensational to send forth a diagnosis of osteogenic sarcoma of the breast than one of mammary carcinoma with osseous and cartilaginous metaplasia. The former has a motif of pleasurable astonishment while the latter is only prosaic.

The therapeutic principles applicable to all infiltrating mammary carcinomas are repeated here.

*Squamous Carcinoma.*—Reference is made to a tumor of the breast proper and not to squamous carcinoma of overlying skin. It might be preferable to list this tumor as infiltrating duct carcinoma with squamous metaplasia since the fuller term is descriptive of its source of origin. Limited and unimpressive areas of a few mammary duct cancers show the traits of squamous carcinoma but usually they are imperfectly developed (Figs. 22 and 23). Cases in which the structure of squamous carcinoma predominates and those which show keratohyaline granules, intercellular bridges, and epithelial pearls are a great rarity, too few to express practically in terms of per cent. Use of the term squamous carcinoma may be thought proper when there is a major degree of this sort of structure or when this is the sole structural form seen. As a compromise it is suggested that diagnosis in this group be recorded as infiltrating duct carcinoma growing partly (or largely) as squamous carcinoma. No case has come to our attention of a primary tumor of this sort that was purely squamous. Invariably there have been areas showing transition from duct carcinoma of not unusual

sort. Once in a great while, in a series of local recurrences, the structure in a biopsy may be solely that of squamous carcinoma. This structural change has never been traced in lobular carcinomas but it cannot be excluded as a theoretic possibility since acanthosis is a common variant in a great many carcinomas in widely divergent locations. On theory one may speculate on the possible existence of noninfiltrating squamous carcinoma of the breast.

Fig. 21.

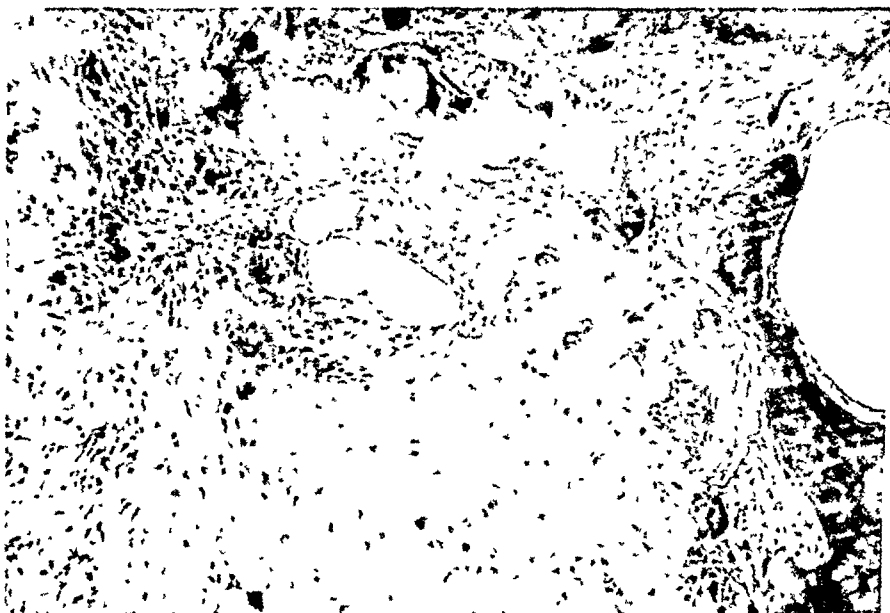


Fig. 22.

Fig. 21.—Mammary carcinoma with cartilaginous and osseous metaplasia.  
Fig. 22.—Infiltrating duct carcinoma growing partly as epidermoid carcinoma.

No specific gross features typify this histologic type of tumor, but as a general rule they are relatively large.

*Malignant Variant of Fibroadenoma and Cystosarcoma Phyllodes.*—The frequency of these tumors is such that they are practically museum curiosities. The differences between intracanalicular fibroadenoma and cystosarcoma

Fig. 23.

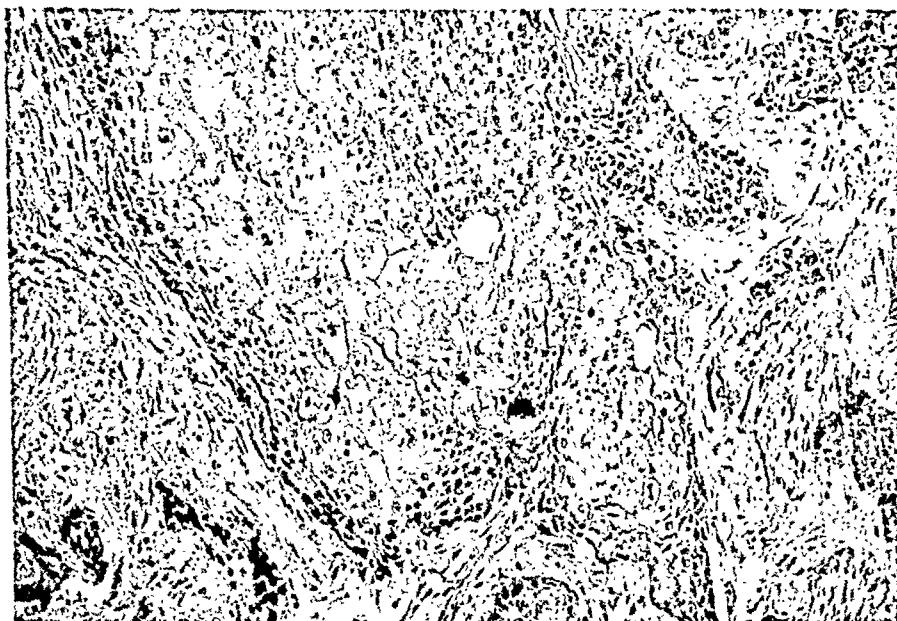


Fig. 24.

Fig. 23.—Mammary carcinoma which has assumed properties of squamous carcinoma.  
 Fig. 24.—Malignant phase of cystosarcoma phyllodes; death with lung metastases.

phyllodes are principally those of size—the size of the tumors as a whole as well as the size of the individual intracanalicular components. Indeed, the initial publication on cystosarcoma phyllodes by Johannes Müller referred to this tumor as giant intracanalicular fibroadenoma. Thus, when one is confronted by a huge encapsulated tumor with gigantiform intracanalicular projections, no uncertainty exists as to the applicability of the term, cystosarcoma phyllodes. These tumors, however, descend from this level of great mass until they are only a few centimeters or less in diameter. The smaller tumors, nevertheless, may present coarser than usual intracanalicular protrusions whose connective tissue portions are more cellular and whose overlying epithelium is more proliferative than that seen ordinarily in intracanalicular fibroadenoma. The question of terminology is provoked and in this laboratory the term “miniature cystosarcoma phyllodes” has been adopted. It is thought that this is more than a pure academic word problem since the tumors have at least a limited capacity for recurrences and these can assume malignant form. An added feature is that they are likely to occur at an older age than is expected for fibroadenomas in general. Compactly stated, the differences between intracanalicular fibroadenoma and cystosarcoma phyllodes concern size and cellularity. In passing it is mentioned that the term cystosarcoma phyllodes without qualification should not denote a malignant tumor. The term is in itself an unfortunate one. Certainly all giant intracanalicular fibroadenomas are not malignant clinically or histologically and when the synonym cystosarcoma phyllodes is used it should imply a benign tumor unless further qualified as malignant or malignant variant.

When a giant intracanalicular fibroadenoma passes into a malignant phase the change involves the connective tissue and not the epithelium in the great majority of cases (Fig. 24). Observation of a considerable number of tumors in an early phase of malignant transformation is the basis for this belief. In the exceptional case both types of cells participate in the malignant process and it would be proper here to speak of true adenosarcoma or carcinosarcoma, that is, adenosarcoma in the derivative sense. Supporting this view of histogenesis is the clinical behavior of the tumors. Those tumors growing as spindle- and polyhedral-cell sarcoma customarily cause death resulting from bulky lung metastases and do not yield axillary node metastases. Cases that develop node metastases are those in which malignant epithelial characters are demonstrated.

A very small number of these tumors develop bizarre structural patterns which include those of squamous carcinoma and osteogenic sarcoma with formation of atypical bone and cartilage.

If a histologic diagnosis of the malignant phase of these tumors is made, there are certain therapeutic implications. If the tumor contains malignant epithelial cells, radical mastectomy is needed. If painstaking study reveals only malignant connective tissue cells, simple mastectomy may be employed. If doubt exists on these points, as sometimes it does, the radical procedure seems a prudent course. In all probability this should always be done when the

tumor has extended beyond its capsule. Confinement within the capsule is naturally a favorable factor but we have witnessed the development of lung metastases when there was no demonstrable invasion of adjacent breast tissue, presumably the result of blood stream invasion within the body of the tumor.

When the common intracanalicular fibroadenoma undergoes malignant change it usually does so in a fashion converse to that usual in cystosarcoma phyllodes. Hence it is the epithelial portion that is concerned rather than connective tissue component. This cannot be regarded as an invariable rule but is a major trend. Malignant fibroadenomas are among the rarest of malignant neoplasms of the breast, somewhat less frequent than the malignant variant of cystosarcoma phyllodes. It may be that malignant fibroadenomas are commoner than can be demonstrated pathologically since a small fibroadenoma could become completely overgrown and obliterated by the malignant tumor cells. On the other hand, a carcinoma developing adjacent to a fibroadenoma can invade the substance of the benign tumor so that a false impression of its origin in that location is imposed. Admittedly, the issue of origin cannot be stated with certainty in some cases.

If the malignant alteration of a fibroadenoma is met with in an early phase, confined to the lining epithelium, or at most not extending beyond the capsule, the disease can be controlled by local excision or simple mastectomy depending upon the extent of the change. With infiltration radical mastectomy becomes necessary.

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## A TECHNIQUE FOR RADICAL MASTECTOMY\*

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**B**ECAUSE radical mastectomy is an extensive surgical procedure in which a series of related regional dissections are required, it is only natural that many different techniques have been developed during the fifty years that the operation has been done. A number of these techniques have emphasized different skin incisions, and some surgeons plan their whole procedure in relationship to the limitations of the skin incision. We believe that it is far more important to emphasize certain principles which are basic in the surgical attack of all malignant disease. Our purpose in describing another method for radical mastectomy is to stress the importance of these principles and to illustrate how they may be applied at every stage of this complicated operation.

The history of the development of the operation has been well described by Willy Meyer<sup>1</sup> and by Cooper<sup>2</sup> and the reader will find their papers well worth studying. Both Halsted and Willy Meyer, who independently devised the modern operation half a century ago, changed and improved their respective techniques as time went on. The operation evolved in their hands until both operators emphasized four common principles:

1. Excision of the skin over the whole breast, covering the defect which remained with a Thiersch graft
2. Excision of both pectoral muscles
3. Complete axillary dissection
4. Removal of the excised tissues in one block.

Since their day, improvements in anesthesia and in methods for the avoidance of shock have made extensive surgical dissections safer. It is today possible to carry out with a reasonable degree of safety an even more radical mastectomy than that which Halsted and Willy Meyer performed. In our own surgical attack on carcinoma of the breast we have followed the fundamental principle that the disease, even when confined to operable limits, is such a formidable enemy that it is our duty to make our dissection as radical as possible. By this we mean that today we attempt to remove as much tissue from the chest wall and the axilla as we dare, without unreasonable danger to the patient's life and interference with thoracic and arm function. Just what these limits are we shall attempt to describe. We eschew at the outset all temptation to compromise with carcinoma of the breast by limiting our operation in any way or by doing simple mastectomy. In the face of the proved fact that carcinoma of the breast that has metastasized to the axilla

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has been cured by radical mastectomy, the performance of simple mastectomy in a patient who can tolerate a radical operation is nothing less than surgical cowardice.

A second fundamental principle which we emphasize in operating upon cancer of the breast is gentleness. We take great care not to press upon the tumor. We avoid traction on the breast. All of our manipulations are as gentle as possible. In our microscopic studies we have seen emboli of cancer cells in the lymphatics and in the peripheral sinuses of lymph nodes often enough to be convinced that such emboli may be set free by rough operating and implanted in the wound.

Our own technique for radical mastectomy has been based upon the Halsted operation, but many of the details are derived from the technique of Dr. George H. Semken. His carefully planned and meticulous methods of surgical attack in several forms of cancer have been our inspiration for special emphasis on this form of surgery. We must acknowledge also our indebtedness to Dr. Allen O. Whipple for apprenticeship in silk technique, which adds, we believe, to the delicacy and exactitude of radical mastectomy.

#### SELECTION OF THE PATIENT

In a recent publication,<sup>3</sup> we have dealt in some detail with the question of operability, presenting a series of criteria for selecting the operable cases. Within the limits of these criteria we believe that women of all age groups with carcinoma of the breast, who are in good enough general condition to run the risk of major surgery, should be treated by radical mastectomy. With such a formidable disease as carcinoma of the breast there is little place for compromise. The operation must be done if the patient can stand it. With proper precautions to avoid shock we have found that we can carry out our complete radical mastectomy with safety upon women in their late seventies and upon women with severe hypertension or diabetes. Patients with severe asthma or chronic bronchitis give us some trouble in the form of respiratory complications, but even with these, operation is certainly indicated.

#### THE ANESTHESIA

For the type of radical mastectomy which we perform we need a method of anesthesia which will maintain the patient at a relatively superficial plane of anesthesia over a period of between five and six hours of operating. Muscle relaxation is not required. We do not mind, in fact, if the patient stirs slightly now and then, for this assures us that she is lightly anesthetized. Prolonged deep anesthesia is shocking and hazardous.

Avertin given by rectum is the basic anesthetic which in the past has best met our needs. It is important to precede the basic anesthesia by at least one hour with premedication which will allay the patient's apprehension. We give 10 mg. of morphine and 0.4 mg. of scopolamine. The avertin is always supplemented by nitrous oxide or ether, and by additional doses of morphine given at intervals during the course of the operation.

We do not give avertin to patients with marked hypertension, because we fear that the sharp fall in blood pressure which the drug produces may cause cerebral injury. We do not use it when there is hepatic or renal damage because of the danger of improper elimination. Cyclopropane or ether is preferable in both of these types of patients.

Recently we have been using with satisfaction a combination of pentothal and nitrous oxide. This anesthesia has the advantage of avoiding the initial drop in blood pressure which is noted with avertin. After pentothal, moreover, the patients waken more quickly and are able to take fluids sooner. The total amount of pentothal should be kept as low as possible.

#### THE POSITION OF THE PATIENT ON THE OPERATING TABLE

There are certain details regarding the position of the patient on the operating table which are worth mentioning. Both arms are outstretched. The skin of the one on the tumor side is, of course, prepared down to the elbow, and the whole arm wrapped in sterile towels so that its position can be changed without breaking its sterility. It is then laid outstretched upon a narrow arm board. The other arm is fastened down to an arm board, and is used for blood pressure readings and for intravenous medication.

The operating table is raised high enough so that when the operator stands erect the operative field is at elbow level. Many an operator works with the table too low, requiring him to bend over. His head gets between his field and the overhead light, and in long operations, such as we are here describing, his back is strained.

The operative table is tilted laterally, raising the side being operated upon about 30 degrees. This makes the lateral chest wall more accessible, and facilitates the dissection of the lateral skin flap, which is the first step in our operation.

#### STEP 1. THE DISSECTION OF THE SKIN FLAPS

We begin by outlining the incision on the skin, using a steel pen and methylene blue for ink. The extent of the skin excised varies with the position and size of the tumor but it is governed by two basic principles. We include the skin over the whole of the protuberant breast (Fig. 1). An additional area of skin is included if the tumor is excentrically situated. When it is in the upper outer sector of the breast, for instance, we include an additional area of skin over the anterior axillary fold. We try to place the line of skin incision at least four fingerbreadths, that is about 7 cm., beyond the edge of the palpable tumor. When the tumor is situated high in the upper outer sector this is sometimes difficult to do for we must retain enough of a skin flap to cover the axillary vessels, so we place our incision a little closer to the edge of the tumor. Other situations of the tumor in the breast do not limit our skin removal. Thus, for tumors of the lower inner sector we include a considerable area of skin over the upper abdomen, extending sometimes to the midline or across it.

We do not plan the extent of skin removal with any reference to closing the wound (with the single exception just mentioned of tumors high in the upper outer sector). We know that we can cover a defect of any size with a skin graft, so we sacrifice as much skin as we think desirable from the viewpoint of curing the carcinoma. The result has been that in every instance we have had a defect of varying size left when the flaps are finally approximated. Since we know at the outset that we are going to have to do a skin graft we are not tempted to skimp in the matter of sacrificing skin.

The actual outline of the skin incision is made by drawing a circle around the breast and the tumor. The circle is then transformed into a vertical incision by pointing it below with a line drawn in the direction of the umbilicus and above with a line drawn approximately in the strap line over the shoulder to a point slightly cephalad to the clavicle.

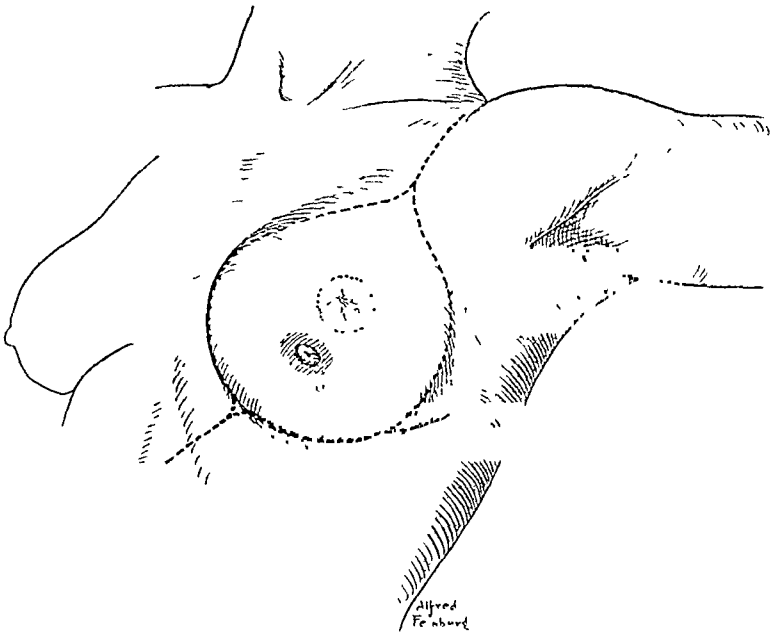


FIG. 1.—The outline of the skin incision.

We formerly carried the upper end of the skin incision out onto the arm over the anterior aspect of the pectoral fold as in the original Halsted and in Willy Meyer's modified (1898) technique. This makes the accurate dissection of axillary flap a little easier, but we have found that this extension onto the arm is by no means necessary. If the incision is carried straight up along the strap-line high up on the shoulder, entirely adequate exposure of the axillary portion of the lateral flap can be obtained with a little careful retraction. The scar is then hidden under the shoulder strap, and the patient can wear a sleeveless dress or a bathing suit.

The worst mistake that the surgeon can make, from the point of view of arm function, in planning the skin incision for radical mastectomy, is to carry the upper end of the incision into the axilla. A vertical band of scar tissue

across the axilla is the inevitable result, and arm motion is restricted. Willy Meyer's original incision extended into the axilla, but he soon realized its disadvantage and changed it.

Transverse incisions are to be avoided because they do not provide adequate exposure of the axilla.

All types of incisions which involve the shifting of flaps to cover the defect that remains when a wide removal of skin is carried out are impractical, because they do not do away with the necessity for skin grafting some area and they further prolong an already lengthy operation.

We dissect back the lateral skin flap first. The incision is made through the skin only, down to the superficial layer of the superficial fascia (Fig. 2). This fascia is delicate but distinct. Over the lower part of the chest wall it is considerably thicker than over the upper part, but with careful hemostasis it can be identified all the way to the upper edge of the operative field at the level of the clavicle. Superficial to this fascia there is only the skin, with its dermal glands and small blood vessels. Beneath it lies breast tissue interspersed in a variable amount of fat. Close beneath the fascia lie the relatively large thin-walled superficial branches of the perforating vessels. They might be called the subfascial blood vessels. Accompanying these blood vessels are lymphatic vessels, which drain the skin over the breast as well as the breast itself.

It is important from the viewpoint of adequate cancer surgery to keep the plane of dissection just superficial to this fascia. First, we wish to be certain that all breast tissue will be removed. We know from our pathologic studies that carcinoma often extends widely throughout breast tissue and that not infrequently it is found as new and separate foci in remote parts of the breast. Breast tissue extends far more widely over the chest wall than the protuberant breast itself. As a thin layer beneath the fascia which we have been describing, breast tissue may be found from the edge of the sternum around the chest wall very nearly to the latissimus dorsi muscle, and from just below the clavicle down to the inframammary fold. It may extend high into the axilla. The surgeon must be certain of removing all breast tissue, and the way to do it is to dissect superficial to the fascia. Second, dissection in this plane will remove the lymphatics accompanying the subfascial blood vessels, one of the routes along which breast carcinoma spreads.

From the viewpoint of surgical convenience also, it is wise to dissect superficial to the fascia. In so doing, the troublesome subfascial vessels will not be cut and the flap can be dissected up leaving hardly any bleeding points on its surface. Good hemostasis makes the dissection more accurate as well as less shocking.

It has been our custom to begin the dissection at the caudad end of the lateral flap and to work toward the cephalad end. The flap is retracted with light sharp, single-pronged hooks which we have devised for this particular purpose. They do not injure the skin as do the various types of compressive

or double-toothed clamps usually employed. In order to provide gentle countertraction in a medial direction on the breast tissue and fat that is being dissected off the skin flap, a series of curved hemostats are placed along the lateral edge of the skin being removed with the breast, clamping the skin edge to a protecting towel which isolates it from the operative field. The handles of the hemostats are tied together in two groups and used as retractors (Fig. 3). In this way rough handling of the tumor area itself is avoided.

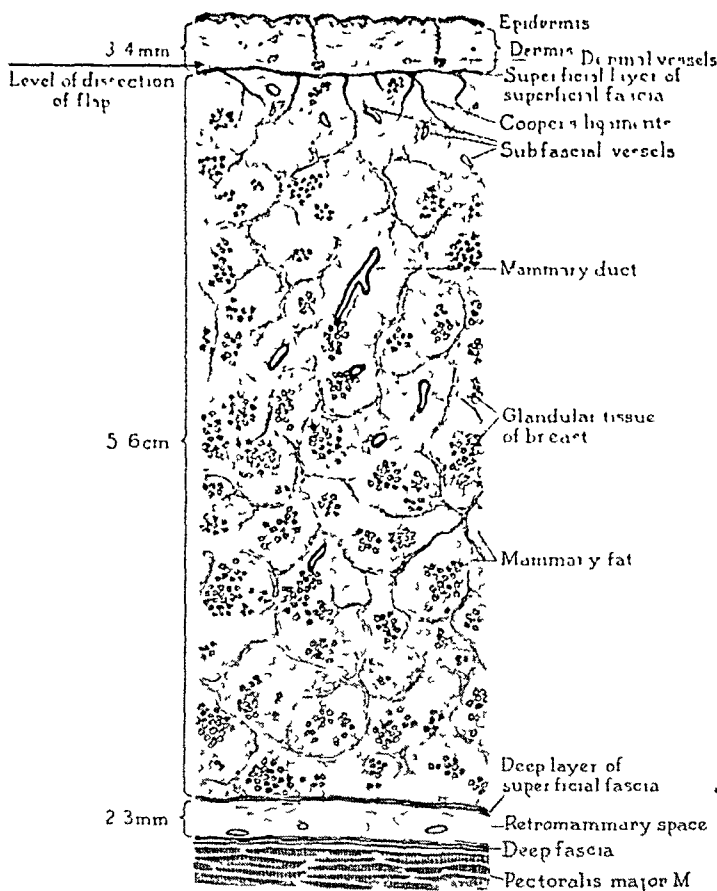


Fig. 2—Diagrammatic cross section through the breast to show the level of dissection of the skin flaps.

Along the caudad portion of the lateral flap the dissection is carried down over the abdomen until a line about four fingerbreadths, or 7 cm, caudad to the inframammary fold is reached. We assume this to be a safe distance from possible carcinoma and turn our plane of dissection directly in toward the body, incising the superficial fascia and exposing the deep fascia over the rectus and external oblique. This gives us what Semken has aptly called a *red line* at the edge of the dissection. It is a definitive guide to what is to be removed. Carried all around the edge of the operative field as the flaps are dissected back, it avoids confusion during later stages of the operation.

We do not remove the rectus fascia except in cases where the tumor is situated in the lower half of the breast. Handley's pathologic evidence<sup>4</sup> of the permeation of this fascia with carcinoma was obtained from far-advanced cases of the type which we would classify today as inoperable.

The red line is carried laterally and cephalad along the base of the skin flap exposing the external oblique and the serratus anterior muscles, and finally reaching the edge of the latissimus dorsi muscle near a point where it crosses the sixth digitation of the serratus. The lateral edge of the latissimus becomes a guide to the operator as the dissection proceeds toward the axilla. Care must be taken not to lose sight of the muscle edge and not to dissect either too far medially into the dangerous carcinoma-containing axillary tissues or needlessly far laterally into the tissues over the dorsal aspect of the latissimus. These errors are easily made, particularly in obese patients.

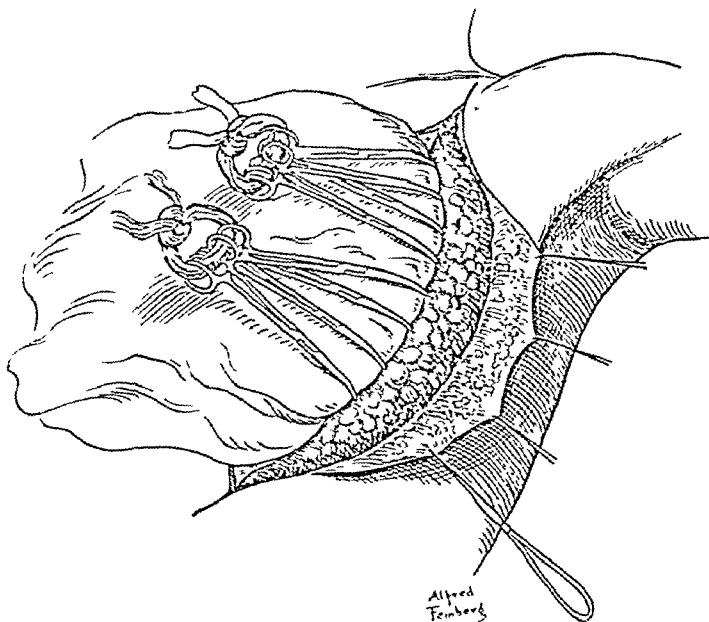


Fig. 3.—Beginning dissection of the lateral skin flap.

At a point about three-quarters of the way upward along the lateral flap this dissection along the latissimus is stopped. The cephalad portion of the skin flap is then dissected up, baring the pectoralis major muscle. This leaves a bridge of axillary fat attached to the skin flap (Fig. 4). This tissue is dissected off of the axillary skin, leaving its apocrine glands exposed. These are seen as small reddish-brown foci of tissue, interspersed with the roots of hairs, lying immediately beneath the skin over the center of the axilla. They are a good guide for the operator in this region, for unless they are exposed the skin flap is being cut too thick. As a final step in the elevation of the lateral flap the dissection is carried cephalad along the white tendon of the latissimus, and then up across the axillary vein (Fig. 5). In this dissection along the

white tendon, carrying our so-called red line up across the axillary vein, several small intercostobrachial nerves and accompanying arteries and veins which cross over the white tendon at right angles to it are encountered. They must be isolated, clamped, cut, and tied with care, otherwise the operative field becomes soiled with blood and good exposure of the axillary vein becomes more difficult.

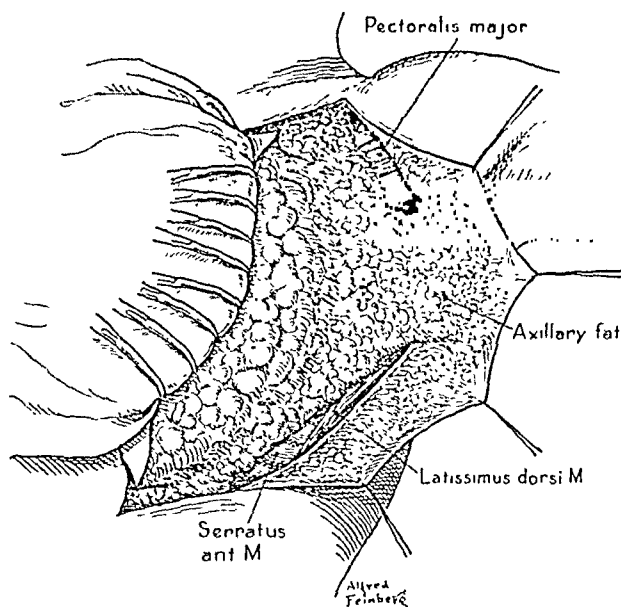


Fig. 4.—Dissection of the lateral skin flap at a later stage.

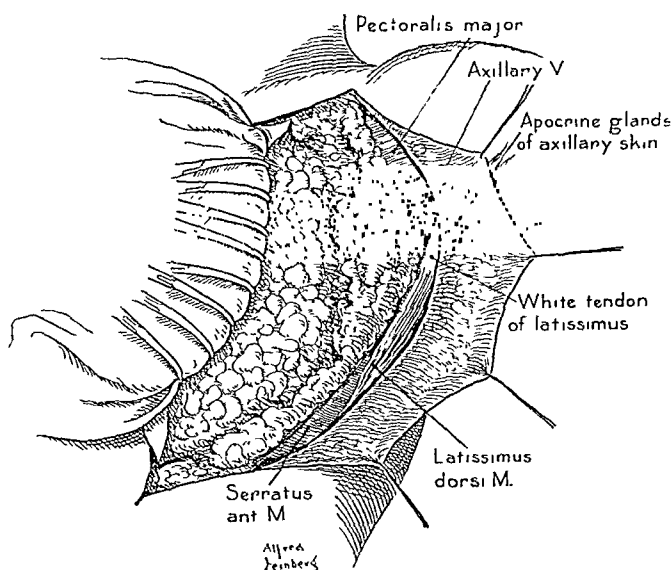


Fig. 5.—Dissection of the lateral skin flap completed.



The hemostasis along the whole length of the axillary flap is now carefully checked, and the flap is replaced against the chest wall so that it will not be angulated and its nutrition interfered with. It is covered with a moist towel. The breast is allowed to fall laterally and the operating table is turned back to a level plane, preparatory to the dissection of the medial skin flap.

The medial skin flap is dissected back with the same technique used for the lateral flap. Again, it is convenient to begin at the caudad end of the flap. The dissection crosses medially over the rectus fascia to reach the midline of the sternum. The red line at the periphery of the operative field is then carried upward along the midline to the inner end of the clavicle (Fig. 6).

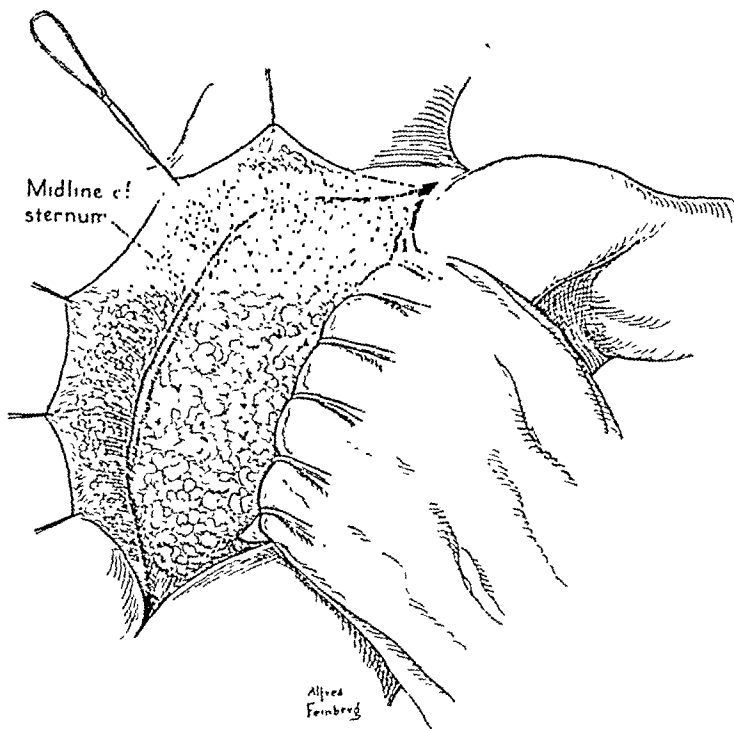


Fig. 6.—Dissection of the medial skin flap.

The direction of dissection then turns laterally and follows the lower edge of the clavicle, encountering fibers of platysma coming down from the neck. Along this clavicular line of dissection a number of small vessels crossing it at right angles require ligation. When the dissection of this medial flap is completed a careful check of hemostasis is made, and it is laid back in place so that it will not be angulated and is covered with a moist towel.

The skin flaps thus dissected up from the superficial layer of the superficial fascia and the breast tissue which lies beneath it are thinner than the flaps that are cut in the usual radical mastectomy. Our flaps are only 3 or 4 mm. thick and consist of the skin covered with only a delicate layer of fine fat lobules. Halsted, in his original operation, dissected this kind of a flap

over the axilla, for he was a good gross pathologist and realized that a thick flap in this region implied dissection perilously close to axillary nodes. Elsewhere, however, his flaps were thick, the incision being carried, in his own words,<sup>5</sup> "through the fat." His original illustration (Fig. 7), which we have reproduced, shows the thin axillary flap turned back, and the deep incision through the fat down to the muscle plane around the periphery of the operative field. In defense of Halsted's technique it must be added that his excision was a very wide one, leaving such a large defect on the chest wall that skin grafting was regularly required.

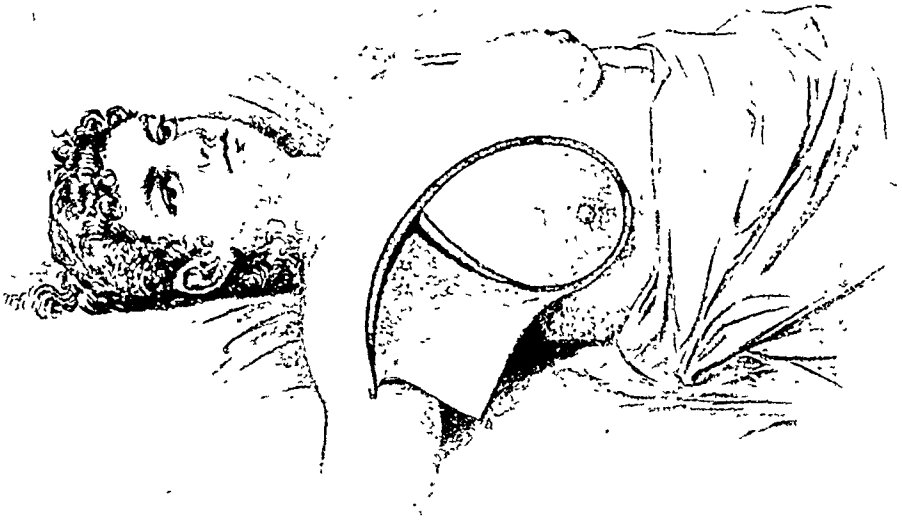


Fig. 7.—The skin flaps as shown in Halsted's original illustration.

Most modern operators are much less radical. Their excision is so limited that the edges of the flaps can be brought together and the wound closed. Moreover, the usual practice is to cut thick flaps around the whole operative field, omitting even the dissection of the thin axillary flap that Halsted emphasized. In Fig. 8, reproduced from an illustration of a contemporary operator's technique, these thick flaps are shown. The skin incision is carried almost directly down through the fat and mammary tissue to the muscle plane, exposing the pectoralis major medially and the serratus muscle laterally. The flaps thus cut bear coarse lobules of fat and are several centimeters thick in most patients. Such flaps are easily and quickly made, while the dissection of our thin flaps is a tedious procedure, requiring between one and one-half hours and two hours. In our technique (Fig. 9) the pectoral and serratus muscles are not laid bare, except where our red line crosses them at the periphery of the operative field. The line of dissection must be exact and the

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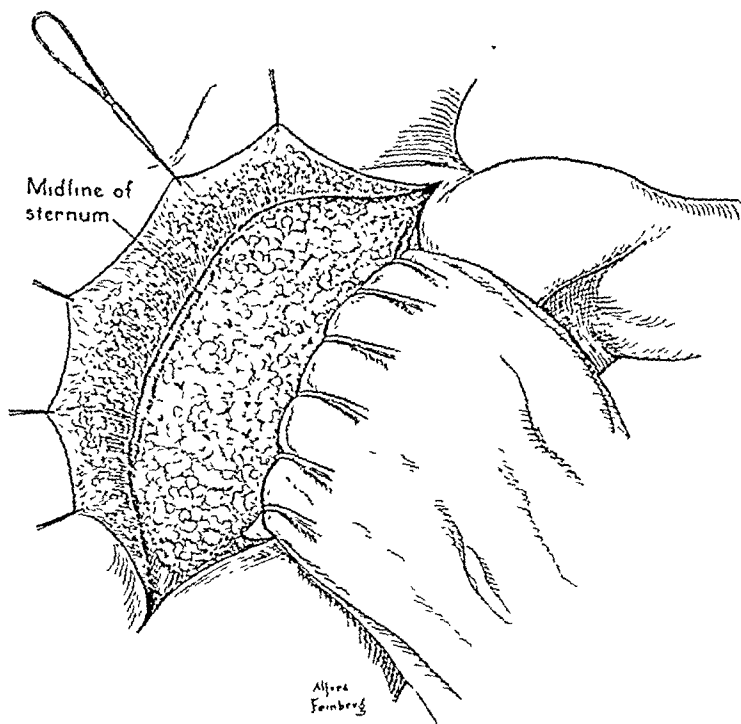


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tissues must be handled gently, otherwise the viability of the flaps will be compromised. We think of this method of dissecting the skin flaps as the logical development of Halsted's original plan. The ultimate value of the method will, of course, depend upon the demonstration of a decreased incidence of local recurrence.

#### STEP 2. THE DISSECTION OF THE PECTORALIS MAJOR FROM THE ARM

The dissection then goes forward at a deeper plane, and we begin by severing the attachment of the pectoralis major to the arm. The surface of the pectoralis at the base of the lateral skin flap over the arm is exposed. With the aid of lateral retraction on the flap the dissection is carried laterally, clearing the muscle surface until the cephalic vein, separating the deltoid from the pectoralis, is identified and exposed. The vein is followed out along the deltoid-pectoral groove until the apex of the pectoralis at its attachment to the humerus is reached. The muscle is then cut across at a right angle to the direction of its fibers, close to its attachment. Only about a centimeter of muscle remains to form a stump which is not bulky and which contains but two or three small vessels requiring clamping and tying. Most operators force a finger beneath the muscle and elevate it before severing it. We do not find this necessary.

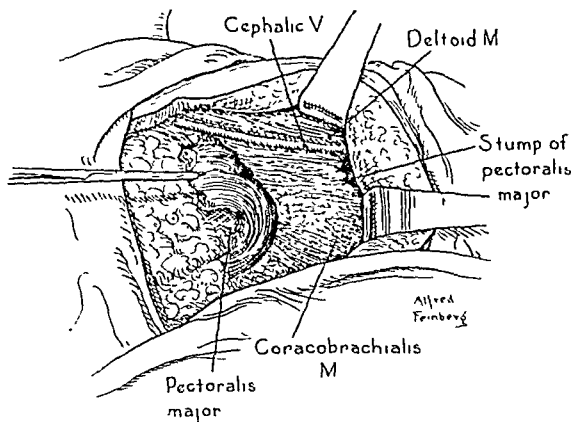


Fig. 10.—Dissection of the pectoralis major from the arm.

When its attachment to the humerus has been cut the pectoralis is dissected free from the deltoid along the cephalic vein and retracted medially, care being taken to clamp and tie the small branches emerging from the pectoralis to enter this vein. The dissection brings the coracobrachialis and the deep pectoral fascia covering the deep structures of the axilla into view (Fig. 10). The operator may be tempted to save the clavicular portion of the pectoralis, splitting the muscle between its pectoral and clavicular divisions. This maneuver has two disadvantages. The line of cleavage is a poor one and bleeding is difficult to control. More important is the fact that leaving the clavicular portion of the muscle in situ hinders proper access to the apex of the axilla.

There are several atypical muscles of the pectoral region, and it is perhaps worth while mentioning the one most frequently encountered and most likely to confuse the operator, the so-called *axillary pectoral muscle*. Eisler's<sup>6</sup> drawing of it is reproduced here (Fig. 11). As a short muscular band of varying thickness, it arches from the white tendon of the latissimus dorsi up over the axillary vessels and nerves to join the tendon of the pectoralis major at its attachment to the humerus. This muscle is well developed in the anthropoid apes and is present in about 7.7 per cent of human subjects of European stock. In the dissection that we are describing it must, of necessity, be severed.

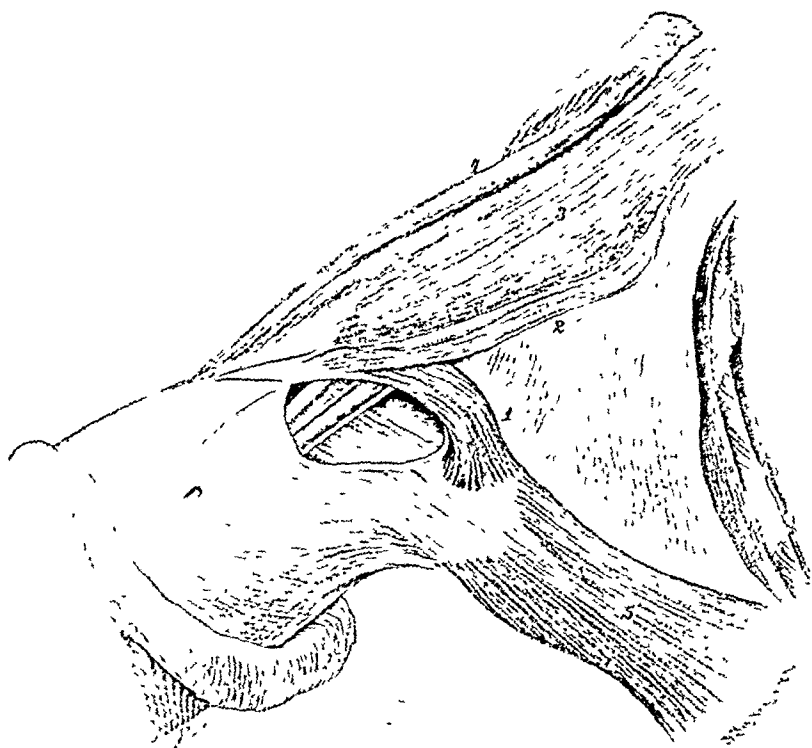


Fig. 11.—Atypical axillary muscles. 1, Axillary pectoral muscle; 2, pectoralis quartus muscle; 3, pectoralis major muscle, sternal portion; 4, pectoralis major, clavicular portion; 5, latissimus dorsi muscle. (From Eisler.)

### STEP 3. THE DISSECTION OF THE PECTORALIS MAJOR FROM THE CLAVICLE

As the dissection of the pectoralis major away from the deltoid is carried medially along the cephalic vein to the apex of the triangle which the deltoid forms with the clavicle, the thoracoacromial vessels come into view. The pectoral branches of the thoracoacromial artery, the accompanying veins, and the lateral anterior thoracic nerve pierce the deep pectoral fascia just above the medial edge of the pectoralis minor, and stretch across the operative field to enter the deep surface of the pectoralis major. They should be carefully isolated, clamped, cut, and tied.

The pectoralis major is retracted caudad exposing the deep pectoral fascia. Beneath this strong fascia lie the pectoralis minor, the axillary vessels and nerves, and the lymphatics and lymph nodes in which we are particularly interested. All of our dissection at this stage of the operation is carried out superficial to this fascia.

The dissection is then carried medially, severing the attachment of the pectoralis major to the clavicle by cutting across its fibers parallel to and about 1 cm. below the lower edge of the clavicle. Leaving a little of the muscle on the clavicle in this way makes it easier to clamp and tie the series of small vessels which are severed. The first interspace is exposed, as the muscle is cut away from its origin on the clavicle (Fig. 12).

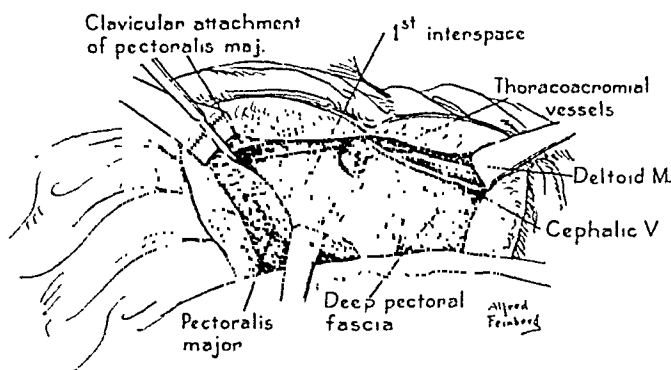


Fig. 12.—Dissection of the pectoralis major from the clavicle.

#### STEP 4. THE DISSECTION OF THE PECTORALIS MAJOR FROM THE CHEST WALL

In this step the pectoralis major is severed from its broad origin from the sternum, ribs, and the fascia of the oblique muscle, allowing the whole operative specimen to fall laterally to the patient's side. This can be the bloodiest and most shocking part of the operation unless it is done with care and exactitude.

The dissection is begun by clearing the first interspace down to the fascia over the intercostal muscles, at a point a little lateral to the medial end of the origin of pectoralis major along the clavicle which was severed in Step 3. The thick body of the pectoralis major muscle is then elevated from the second rib with a small retractor or with the finger, developing a plane of cleavage between this muscle and the thoracic cage. With the muscle thus slightly elevated and tensed its detachment from its broad origin from the inner end of the first interspace, the cartilage of the first rib, and the manubrium is begun. Several branches of the first perforating artery and vein will be encountered as this broad muscle attachment is cut through. The first perforators themselves usually come into view near the caudad edge of the interspace, as they arch up over the second costal cartilage. They should be carefully isolated, clamped, cut, and tied. A much smaller perforating vessel, the first

of a series of minor perforators which emerge parallel to and at a point 3 or 4 cm. lateral to the main perforating vessels, should also be clamped, cut, and tied.

The dissection is then carried caudad, severing the pectoralis from its attachment to the sternum and ribs, and identifying and clamping the perforating vessels as they come into view. Their position in the lower interspaces is variable; sometimes they emerge just below and sometimes just above a costal cartilage. The intercostal spaces should be meticulously cleared of all fat and areolar tissue as the dissection proceeds (Fig. 13). As the thoracic cage is thus denuded it should be covered with warm moist compresses or a towel in order to prevent drying of the tissues and consequent shock. The operative specimen is allowed to fall laterally and is similarly covered with a protecting towel.

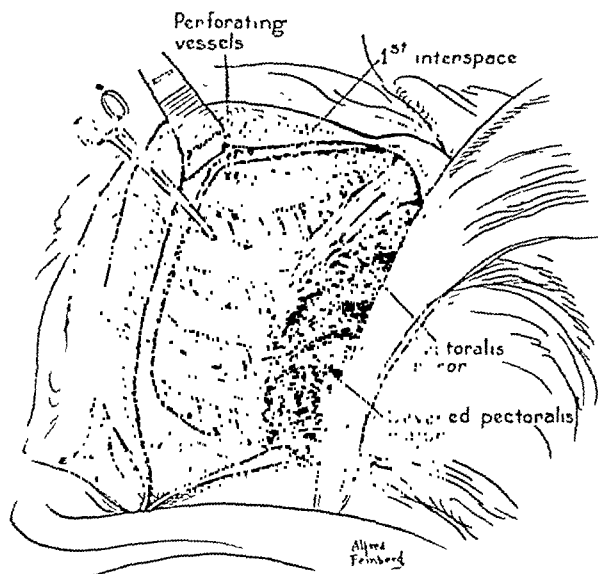


Fig. 13.—Dissection of the pectoralis major from the chest wall.

When the dissection of the pectoralis major from the chest wall has been carried laterally to a point where the fan-shaped edge of the origin of pectoralis minor comes into view, it should be discontinued. This is a convenient point at which to pause and tie the many clamped vessels, getting rid of the mass of clamps that have accumulated as the chest wall has been cleared. The pectoralis minor must now be dealt with in a separate step.

#### STEP 5. SEVERING THE ATTACHMENT OF THE PECTORALIS MINOR

An incision is made through the deep pectoral fascia along the lateral edge of the pectoralis minor muscle near its cephalad end where it becomes tendinous. A finger or a small retractor is gently inserted beneath the muscle, elevating it from the axillary vein and the cords of the brachial plexus which lie directly beneath it.

At this point in the dissection it is desirable to identify, clamp, and cut a tiny muscular branch of the thoracoacromial artery, and its accompanying vein, which usually enters the pectoralis minor along its medial edge near its tendinous end. Although these vessels are very small they bleed freely and obscure the operative field if they are torn in the process of severing the minor.

With the muscle slightly elevated it is cut across as high as is convenient, usually at a point about 2 cm. from its attachment to the coracoid process (Fig. 14). One or two small vessels are severed in its deeper muscular portion. These should be carefully clamped and tied.

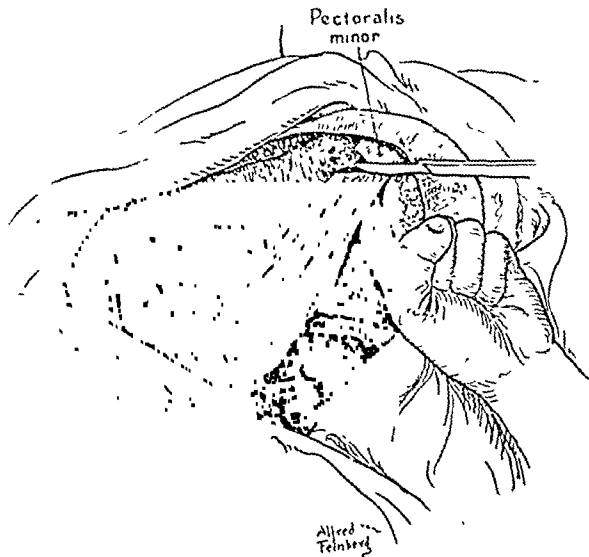


Fig. 14.—Severing the attachment of the pectoralis minor.

The minor is then turned back, exposing its deep surface and baring the areolar tissue covering the axillary structures. Since our axillary dissection is a separate and later step in our operation, we take care not to disturb these axillary structures at this stage. The vessels and nerves which emerge from the areolar tissue of the axilla and stretch across it to enter the deep aspect of the minor are clamped and cut close to the muscle. This frees the muscle so that it can be retracted laterally, giving access to its origin from the third, fourth, and fifth ribs.

#### STEP 6. THE DISSECTION OF THE PECTORALIS MINOR OFF THE CHEST WALL

The pectoralis minor is cut from its origin from the ribs and from the aponeurosis covering the intercostal muscles, proceeding from the third to the fifth ribs. It has been found convenient to pick up the edge of the muscle with thumb forceps and to retract it away from the edge of each rib as its origins are severed. The pectoralis minor interdigitates with the serratus anterior, and special attention is required to distinguish the deeper layers of the minor from the serratus digitations which lie beneath.



The pectoralis minor is allowed to fall laterally with the other tissues severed from the chest wall and the dissection is continued in that portion of the operative field just caudad to the origin of the minor. In this region the dissection of the specimen off the chest wall should include the careful removal of the fascia over the digitations of the serratus (Fig. 15). Important lymphatic trunks, which we will describe later, lie upon or within this fascia.

This dissection is carried laterally around the chest wall, and the specimen allowed to fall away to the patient's side, until the edge of the latissimus comes into view in the caudad part of the field. It is then desirable to suspend the dissection of the specimen off the chest wall, because its detachment can be more conveniently completed after the axilla has been dissected.

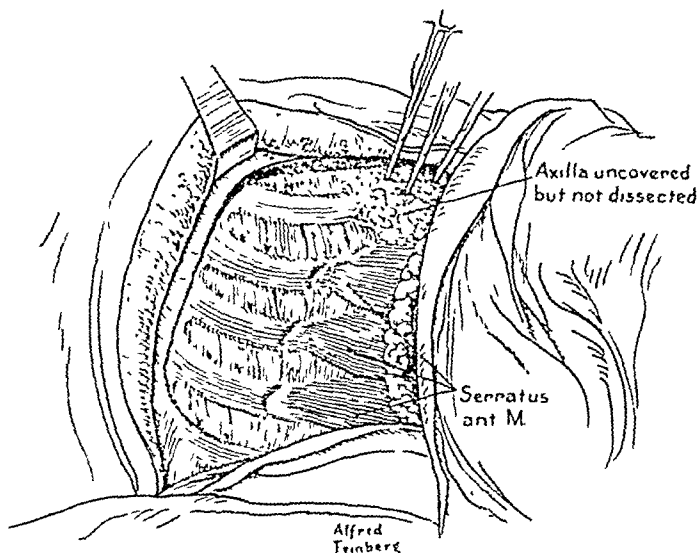


Fig. 15.—Dissection of the breast and pectoral muscles from the chest wall completed.

Before going on to the next stage all clamped vessels on the thoracic wall should be tied, hemostasis checked, and the whole area of denuded thorax carefully covered with moist compresses.

#### STEP 7. THE DISSECTION OF THE AXILLA

The axilla now lies before the operator like an open book. When the arm lies beside the trunk the axilla may be thought of as a cleft between the shoulder structures and the thoracic wall. When the arm is abducted at right angles to the trunk, however, as in radical mastectomy, the cleft becomes a tetrahedral space, with its apex at the clavicle and its base at the pit of the axilla. The three elongated triangular sides of this space are then formed by the shoulder structures cephalad, the chest wall caudad, and the pectoral muscles ventrally. In the usual technique for radical mastectomy in which the axilla is dissected before the pectoral muscles and breast are removed from the chest wall, the surgeon's access to the axilla is not good because the structures forming its ventral wall (the axillary prolongation of the breast and the fat usually found

in this region, and the pectoral muscles) constitute a bulky mass which tends to slide down into the field of dissection in the axilla. In the technique for radical mastectomy which we are here describing, this bulky mass of tissues is out of the operator's way when he attacks the axilla, for with the dissection of the breast and pectoral muscles off the chest wall they have fallen away to the patient's side. Any surgeon who has compared the ease of access to the axilla with these two different techniques will at once realize the advantage, from this point of view, of our procedure. Instead of having to dissect in the depths of a deep narrow cleft, bothered by the need for constant retraction of the overlying tissues, the surgeon can work at ease without any retraction on a comparatively flattened field.

The objection usually voiced against our technique of excising the breast and pectoral muscles from the chest wall before attacking the axilla is that it increases the chance of distant metastasis. We do not believe that this is the case. The axillary route for metastasis, of course, remains open during the period required to dissect the breast and pectoral muscles from the chest wall, but we do this without any handling of the tumor itself and with only the gentlest kind of retraction on the muscles close to the point at which they are cut from the chest wall. It should be emphasized, on the other hand, that in the usual technique for radical mastectomy in which the breast and the pectoral muscles are retracted medially as they are severed from the chest wall, strong traction on the specimen is required and a considerable degree of pressure is often exerted upon the tumor itself. Even though this takes place after the lymphatic pathway through the axilla has been severed we fear that it may squeeze tumor emboli into lymphatic trunks which still remain, such as those to the internal mammary chain of nodes.

As another objection to our technique of excising the breast and pectoral muscles from the chest wall before attacking the axilla, it has been asserted that we cut across the pathway of lymphatic drainage to the axilla in carrying out the first steps of our operation. A review of the anatomy of the lymphatics of the breast will show, however, that we do not disturb the main lymphatic pathway to the axilla, which is by way of lymphatic trunks which run laterally and upward from the breast to enter the central group of axillary lymph nodes. This pathway is beneath the deep pectoral fascia, which remains undisturbed by the first steps of our operation. We unroof the axilla but we do not enter it.

Because no adequate description of the anatomy of the lymphatics of the breast has been presented in English since Leaf<sup>7</sup> included this information in his excellent little book *Cancer of the Breast: Clinically Considered*, printed in 1912, it seems desirable to include such a description here. The best monographs on the lymphatics are those of Bartels<sup>8</sup> and Rouvière<sup>9</sup> but they are not everywhere available. Tobias<sup>10</sup> translation of Rouvière's work is unsatisfactory because of the poor quality of the illustrations. Oelsner<sup>11</sup> and Mornard<sup>12</sup> made special studies of the breast lymphatics which are well worth reading. A thorough understanding of this anatomy is of fundamental importance to the surgeon attacking breast carcinoma.

The main collecting lymphatic vessels from the breast are two trunks which leave the subareolar lymphatic plexus, one from its medial and one from its lateral side, and run laterally directly to the central group of axillary lymph nodes or indirectly to the central nodes by way of the external mammary or the paramammary nodes.

There are, in addition, several accessory lymphatic pathways from the breast as follows:

1. The Transpectoral Pathway. The transpectoral lymphatics penetrate the pectoralis major along the course of the pectoral branches of the thoracoacromial artery, and enter the subclavicular group of nodes. Occasionally intermediary lymph nodes are found along these lymphatic vessels, the so-called nodes of Rotter.

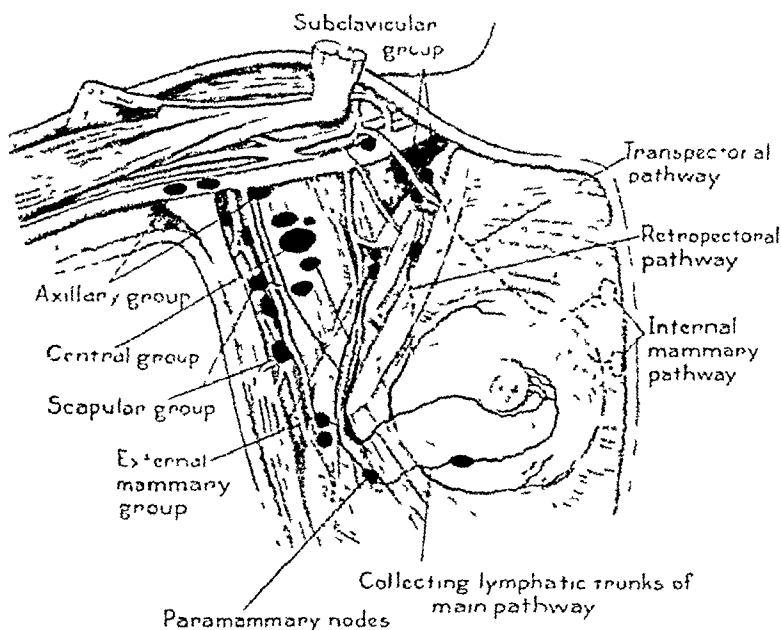


Fig. 16—The lymphatics of the breast

2. The Retropectoral Pathway. One or two lymphatic vessels may turn the outer edge of the pectoralis major and ascend either between the two pectoral muscles or beneath the pectoralis minor, directly to the subclavicular group of nodes.

3. The Internal Mammary Pathway. A series of lymphatic vessels directed toward the midline drains the medial portion of the breast. These vessels accompany the anterior perforating branches of the internal mammary blood vessels, and pierce the intercostal spaces near the sternal border to reach the internal mammary chain of nodes. We are inclined to believe that this is an important route of lymphatic drainage, because we see local recurrence of carcinoma of the breast more frequently just at the sternal edge where these

lymphatics pierce the chest wall than almost anywhere else. We have often noted that the superficial branches of the perforating blood vessels, the ones we have designated as the subfascial vessels, are enlarged at the intercostal level of the breast tumor. Presumably this hypertrophy is due to the increased demand that the tumor makes upon the circulatory system. It is not surprising that correspondingly hypertrophied lymphatic vessels may contain tumor emboli which lodge, for some reason, at the point where these vessels pierce the chest wall, and subsequently become evident as local recurrence of the carcinoma at this point.

In addition to the deeper lymphatic trunks which we have been describing, the breast is, of course, drained by regional cutaneous lymphatics. These form a dense network in several planes over the center of the breast. The most superficial of these planes has been called the areolar plexus and corresponds in position to the dermal lymphatic plexus of the skin. The deeper plane is called the subareolar lymphatic plexus and corresponds to the subdermal lymphatic plexus of the skin. The collecting trunks from these lymphatics of the skin over the breast converge toward the axilla and empty into the central group of axillary lymph nodes. They also anastomose freely with the cutaneous lymphatics of the adjacent skin over the upper abdomen, the neck, and, most important of all, over the opposite mammary region. This anastomosis of cutaneous lymphatics across the midline is the path by which carcinoma extends from one breast to the other.

In passing, we should point out that true metastatic involvement of the opposite breast is ordinarily seen only in the late stage of carcinoma of the breast. In most instances in which the opposite breast becomes involved, and the original disease is not far advanced, we believe that the carcinoma in the opposite breast is a new primary tumor.

We have described elsewhere<sup>3</sup> the process by which carcinoma emboli lodge in the dermal or so-called areolar lymphatics, blockade the flow of lymph from the skin over the breast, and make it edematous. When carcinoma emboli have reached this relatively superficial position the disease is far advanced and the chance of cure remote.

Permeation of the cutaneous lymphatics giving the picture of carcinoma en cuirasse is the final stage in many instances.

In these advanced cases, involvement of the lymphatics of the external intercostal muscles which terminate in the posterior intercostal nodes, and in those of the internal intercostal muscles which terminate in the internal mammary nodes, may occur. Under similar circumstances the lymphatics of the rectus sheath and rectus muscle provide a route for metastases to the triangular ligament and nodes at the hilum of the liver. These lymphatic routes and the variegated types of retrograde lymphatic permeation which occur in advanced carcinoma of the breast are not pertinent to our discussion of the technique of radical mastectomy, because the operation should not be done in advanced cases.

The lymph nodes which the surgeon must attempt to excise en bloc in a radical mastectomy number between thirty and forty in younger patients. In old age their number may be considerably smaller and the bulk of lymphoid tissue greatly reduced by fatty replacement. Our drawing (Fig. 16) showing the position of these nodes has been adapted from Rouvière's, and is semi-diagrammatic.

There are five principal groups of nodes, as follows:

1. The Axillary Vein Group. The axillary nodes lie along the lateral portion of the axillary vein, usually on its caudad aspect.

2. The Scapular Group. The chain of scapular nodes lies along the subscapular blood vessels and extends from the lateral thoracic wall to the axillary vein.

3. The External Mammary Group. The external mammary nodes lie along the medial wall of the axilla, outside of or in the fascia covering the digitations of the serratus anterior muscle. The chain extends from the sixth rib to the axillary vein, following the course of the lateral thoracic artery.

4. The Central Group. The central group are the largest of the axillary nodes and they lie embedded in fat in the center of the axilla. They are the nodes most often palpable. They can best be felt by gentle palpation against the lateral thoracic wall with the arm relaxed and adducted, for in this position the deep pectoral fascia is relaxed and the nodes lie against the chest wall.

5. The Subclavicular Group. The subclavicular nodes lie at the apex of the axilla. They are often found as high as the surgeon can carry the dissection, at the point where the subclavian vein disappears beneath the subclavius muscle. The collecting trunks from all of the other groups of axillary nodes empty into these subclavicular nodes, and from the plexus of lymphatic vessels which connects them one with another, one or more large lymphatic trunks arise which pass upward beneath the clavicle to empty into the junction of the jugular and subclavian veins. These large trunks can be plainly seen at the very apex of the axilla, especially where the nodes contain metastases and the lymphatic trunks are enlarged.

All of the nodes that we have been describing lie beneath the deep pectoral fascia which encloses them together with the axillary blood vessels, nerves, connective tissue, and fat, within a delicate yet strong sheath. This fascia has been variously called the suspensory ligament of the axilla, the costocoracoid membrane, the clavicoracoaxillary aponeurosis, etc. We have reproduced Eisler's<sup>13</sup> excellent drawing of it (Fig. 17). Whatever name is given to it, surgeons should recognize its importance as a guide in the dissection of the axilla. As Leaf has pointed out, this fascia gives coherence to the fat and lymph nodes of the axilla and makes their removal in one piece, together with all of the fascia, easier than would otherwise be the case.

The pectoralis minor, in its vertical course across the middle of the axilla, lies between two planes of the deep pectoral fascia. It is, therefore, quite impossible to dissect the axilla adequately without sacrificing this muscle.

Between the cranial edge of the minor and the clavicle is an irregular four-sided space surrounded by bandlike thickenings of the deep pectoral fascia. There is usually a central fossa ovalis in this space providing an opening in the fascia through which the anterior thoracic vessels and the cephalic vein pass.

Between the lateral edge of the pectoralis minor and the coracobrachialis muscle there is a three-sided space covered by a particularly strong portion of the deep pectoral fascia.

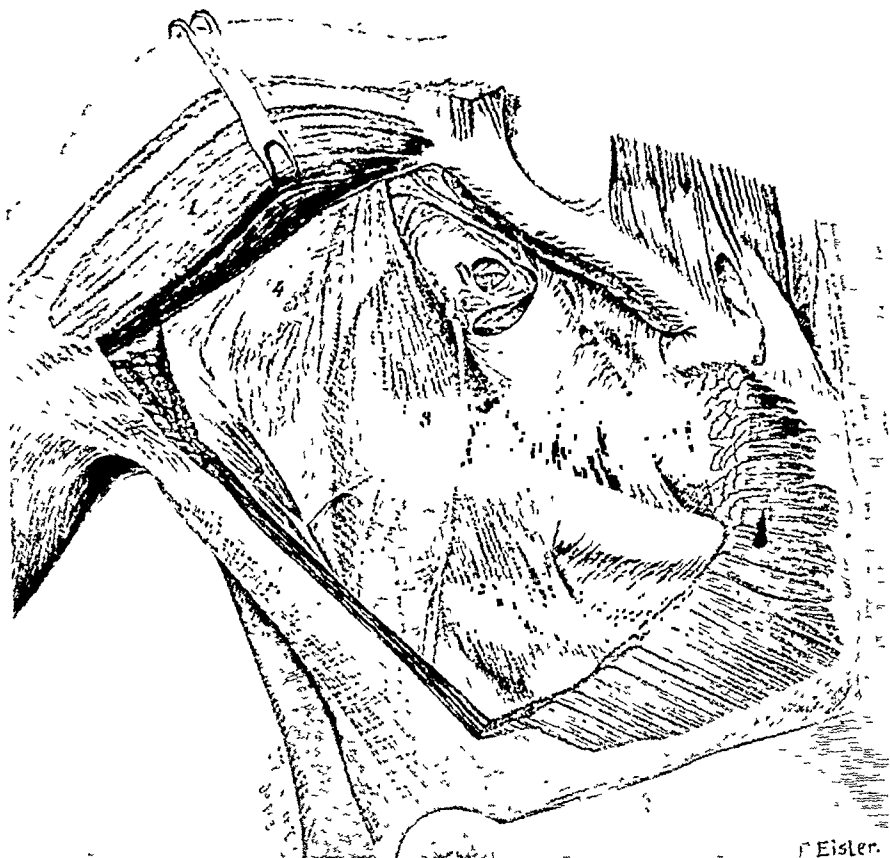


FIG. 17.—The deep pectoral fascia as shown after the pectoralis major has been to a large extent removed. 1, Deltoid, 2, pectoralis major, 3, pectoralis minor, 4, coracobrachialis. (From Eisler.)

We begin our dissection of the axilla by incising the deep pectoral fascia over the brachial plexus, parallel to and slightly cephalad to the axillary vein (Fig. 18). The fascia is picked up between smooth forceps held by the operator and by his assistant, and incised with a sharp knife. All of our axillary dissection is done with smooth forceps and the knife. We never scrape the axillary contents out with a gauze sponge over the finger as is the custom of some operators; if the nodes contain metastases this is a splendid way to implant carcinoma cells throughout the operative field and to insure local recurrence. We use smooth rather than toothed forceps in our dissection because we fear that toothed instruments may pierce carcinomatous nodes and pick up

and reimplant carcinoma cells. We take care, indeed, to avoid grasping nodes even with smooth forceps. Very little traction is needed and usually it can be exerted through clamps on the specimen side of the vessels that are divided.

The deep pectoral fascia having been incised above the vein, the fascia thus released and the fat and areolar tissue attached to it are dissected caudad, bringing the wall of the vein into view. Its ventral and caudad surfaces are meticulously cleared from the level of the thoracoacromial vessels laterally to the point where the vein crosses the tendon of the latissimus. The branches of the vein are isolated, clamped, cut, and tied as they are encountered. They vary greatly in number and arrangement. Only one thing need be kept in mind: they should all be sacrificed. The axillary vein occasionally divides into two main trunks. These, of course, should both be preserved. We have not found it necessary to sacrifice the axillary vein on account of the extent of the axillary metastases. Proper care in the selection of cases for operation will avoid the necessity for such a radical and futile step, for we are convinced that such cases are incurable.

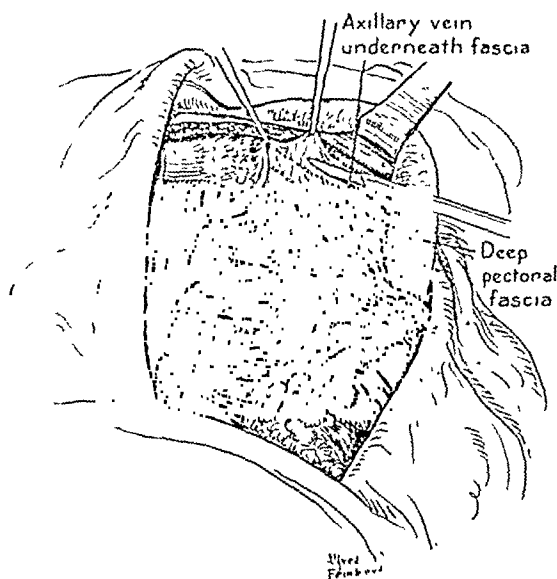


Fig. 18.—Beginning the axillary dissection.

It is not necessary to dissect the fat and areolar tissue overlying the brachial plexus. The axillary lymph nodes are not found lying cephalad to the axillary vein, except in the vicinity of the thoracoacromial vessels. We have occasionally found one or two nodes in this region and it is therefore our custom to clear the stumps of these vessels with care.

A technical detail concerning the dissection of the axillary vein is worth mentioning. At a point from 1 to 3 cm. lateral to the thoracoacromial vessels beneath the portion of the vein uncovered by the removal of the pectoralis minor, the vein is usually crossed obliquely by a small artery and nerve (Fig. 19). The artery enters the deep surface of the pectoralis minor and sometimes

sends a branch onto the adjacent chest wall. Its origin is hidden above and behind the vein where the surgeon does not see it, but it is from a common trunk with the thoracoacromial axis in about one-half of the anatomic subjects we have studied, and as a separate branch from the main artery, 1 or 2 cm. lateral to the thoracoacromial trunk, in the other half of the subjects. It is not described in the anatomic texts which we have consulted, so that we have had to designate it simply as *the artery to the pectoralis minor*.

The nerve which accompanies it is the medial anterior thoracic nerve, which also supplies the pectoralis minor. Both the artery and the nerve are closely applied to the ventral surface of the vein in their oblique course across it, and it is from this fact that their importance to the surgeon arises. Since we strip the axillary vein clean we necessarily remove these two structures which cross over it. A small vein is usually found emptying into the axillary vein just beneath the crossing artery. In isolating, clamping, and cutting the artery and nerve, care should be taken to identify and clamp this small venous branch before it is torn and the operative field soiled with blood. It is possible indeed to dissect the entire axilla without any loss of blood, the great advantage being that the surgeon can see all the time exactly what he is doing.

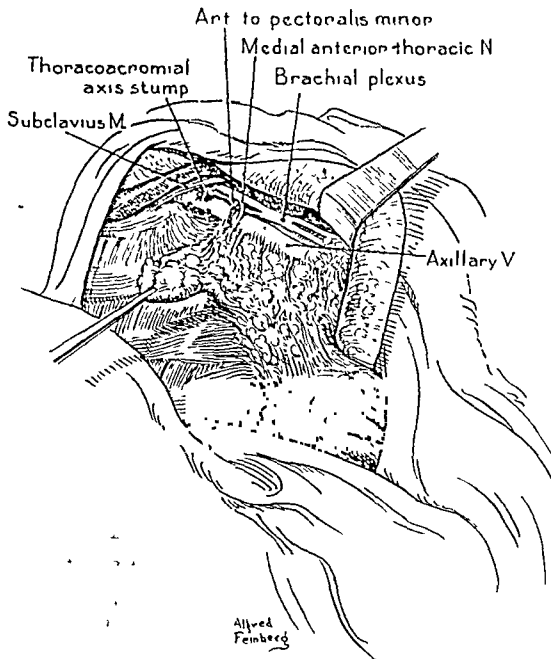


Fig. 19.—Clearing the axillary vein.

Having cleared the ventral and caudad aspects of the axillary vein, we turn our attention to the apex of the axilla. We dissect the fat and areolar tissue off the subclavian vein to the point where it crosses beneath the subclavius muscle. The reflection of the deep pectoral fascia onto the chest wall opposite this portion of the vein is then dissected away from the chest wall to the apex



of the axilla. The mass of fat and areolar tissue thus mobilized in the cleft between the chest wall and the vein contains the highest axillary lymph nodes and the lymphatic trunks that pass upward beneath the clavicle to empty into the venous circulation. A clamp is placed across the apex of the mass as high as possible and it is cut across and ligated in order to avoid backflow of lymph into the wound and to secure the small blood vessels which are usually included within the clamped tissue. A long marking tie is placed around the free end of the mass of apical tissue to orient the pathologist in his study of the specimen.

In order to avoid injury to the long thoracic nerve during the next stage of the axillary dissection, it is now desirable to continue the dissection of the tissues from the chest wall, already begun at the apex of the axilla. The sheet of fascia over the digitations of the serratus anterior is gently retracted laterally and dissected off this muscle. The intercostohumeral nerves spanning the axilla transversely, and the lateral cutaneous branches of the intercostal nerves and their accompanying vessels, are encountered and ligatured, as this dissection is carried dorsally. In the depths of the cleft between the naked serratus digitations and the sheet of fascia retracted laterally, the long thoracic nerve of Bell finally comes into view. It lies in the fat just beneath the surface of the fascia (Fig. 20). An incision is made through the fascia along the lateral edge of the nerve and it is allowed to drop back medially out of the way of subsequent dissection.

We return again to the axillary vein and complete its dissection, beginning at its medial end. The vein is lifted up with a small vein retractor and its branches clamped, cut, and tied one by one as the dissection proceeds laterally. The mass of tissue between the vein and the chest wall is dissected downward and outward off the surface of the subscapular muscle, leaving the long thoracic nerve as the only structure crossing the medial part of the axilla in a longitudinal direction.

When the dissection of the tissues from the subscapular muscle reaches a point where the thoracodorsal nerve is encountered as it arches down from beneath the axillary vein to join the subscapular vessels, a decision has to be made whether to sacrifice or to preserve it. We have pointed out that this nerve, during the last 6 or 8 cm. of its course before it enters the latissimus muscle, lies among the lymph nodes of the scapular group. In our opinion it is unreasonably hazardous to dissect the nerve out from among these lymph nodes if it seems likely that they contain metastases. If palpation of the axilla has suggested lymph node involvement or if, in the course of the axillary dissection up to this point, there has been any gross evidence of axillary metastases, we sacrifice the thoracodorsal nerve forthwith. The paralysis of the latissimus which results, with weakness of abduction and internal rotation of the arm, is not a serious handicap.

If the nerve is preserved it is drawn medially and dissected away from the subscapular vessels.

The subscapular vessels themselves are regularly sacrificed in our technique. They are clamped, cut, and tied just beyond the point where the scapular circumflex branches are given off, usually 3 or 4 cm. from their origin.

The axillary vein having been cleared all of the way out to the point where it crosses the outer edge of the latissimus dorsi muscle, the mass of axillary tissues, now freed from all of its medial and cephalad connections, is dissected in a caudad direction down over the surface of the pyramidal muscle body formed by the subscapularis medially, and the teres major and the latissimus dorsi laterally. If the thoracodorsal nerve, as well as the subscapular vessels, has been sacrificed this part of the dissection is quickly done.

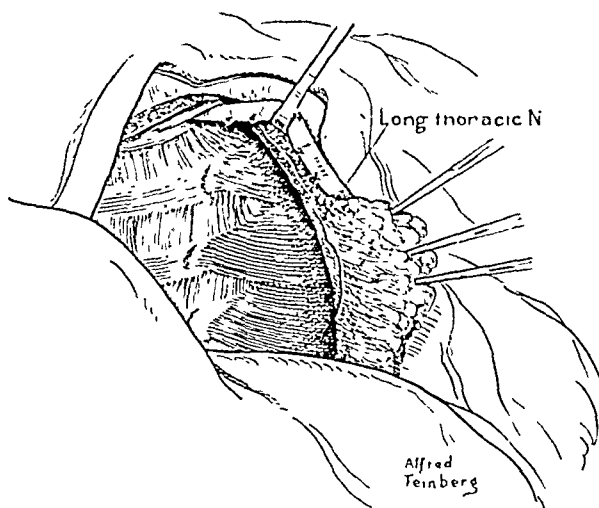


Fig. 20.—Dissecting the medial aspect of the axilla.

The final step in the axillary dissection is the excision of the specimen from along the groove between the chest wall and the latissimus dorsi, its only remaining attachment. This is carried out along a longitudinal plane and from the chest wall toward the latissimus as shown by the arrows in Fig. 21. More ventrally the dissection along this plane had included the removal of the fascia over the serratus, but when, in this final stage, the dissection reaches the level of the long thoracic nerve as it lies upon the serratus fascia, the operator must take care to dissect more superficially in order not to damage the nerve.

When the medial aspect of the latissimus dorsi is reached the plane of dissection is turned laterally. A little outward traction on the specimen as it lies on the table at the patient's side enables the operator to roll, so to speak, the remaining tissues laterally over the latissimus dorsi. In this process the branches of the subscapular vessels which turn medially to supply the chest wall opposite the apex of the subscapular and teres major muscle body, as well as those which enter the latissimus itself, are isolated, clamped, and ligated. These vessels are of considerable size, and the region has been aptly called the

“bloody angle” of radical mastectomy. With the technique which we have described here, however, there is no need of any hemorrhage, for the surgeon’s access is good and the vessels easily identified.

To complete the dissection, the specimen is cut free from the edge of the latissimus dorsi. The operative field, as it appears at the end of the dissection, is shown in Fig. 22.

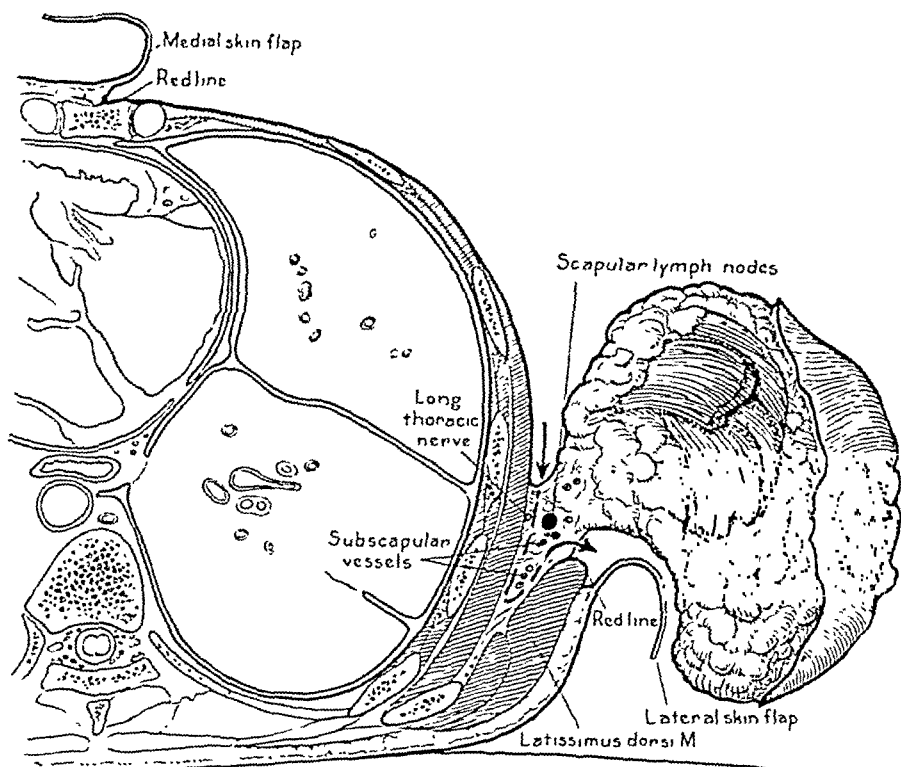


Fig. 21.—The final step in the dissection.

#### STEP 8. THE CLOSURE OF THE WOUND

We carefully inspect the whole extent of the wound, to be sure that it is dry, for if it is to be closed without draining, as is our custom, hemostasis must be meticulous.

The skin flaps are then replaced on the chest wall and sutured together at the upper and lower ends of the wound with interrupted sutures of B silk on fine straight needles. The suturing is carried only as far as the flaps will come together without excessive tension. By this we mean a degree of tension which will cause necrosis. Our flaps are so thin that the amount of tension required to damage them is not great. The operator has to learn by experience what is safe. Blanching of the skin of the flap beyond the suture is the best sign that too much tension has been used.

A defect of varying size remains. This is rarely less than 12 cm. in diameter, and is often considerably larger. The edges of the skin flaps around

the defect are sutured down to the chest wall with interrupted sutures of silk, their ends being left one inch long and laid out on the surface of the flaps so that they can be easily picked up from beneath the overlapping edges of the skin graft when it is time to remove them, (Fig. 23). In suturing the edge of the lateral flap to the chest wall to make the required even curve, it is often necessary to pucker the edge a little between the sutures, but this straightens out very well in the healing process.

The defect is covered with a Thiersch graft, which is usually taken from the outer surface of the thigh. Since it is quicker to cut the graft by hand than with the dermatome we usually use the former method. If the operator is unable to cut a large enough graft with the Blair knife to cover the defect in one piece he had best use the dermatome. The graft should overlap the edges of the flaps slightly, so that a continuous suture of silk can be placed through it around its edge, fastening it securely to the underlying flap edges. It is then covered with a single layer of xeroform waxed gauze.

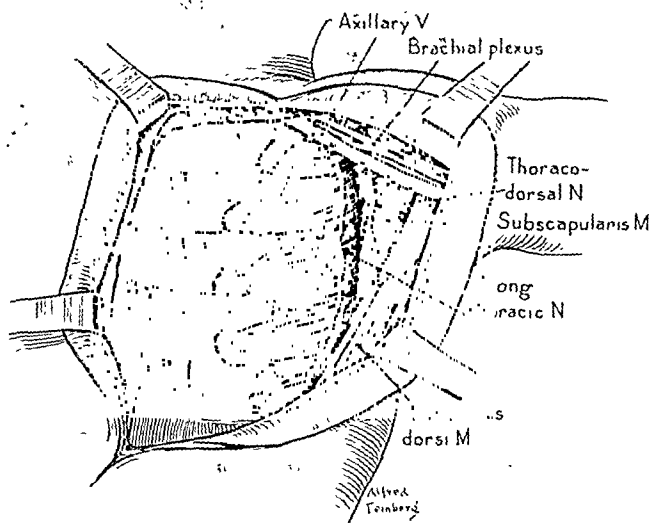


Fig. 22.—The operative field at the end of the dissection.

No drain is used. We have found that if hemostasis is meticulous none is required. In perhaps one-fifth of our patients a small accumulation of serum beneath the axillary end of the lateral flap results. One or two aspirations of the serum are required, but we regard this as a lesser evil than drainage. The use of a drain favors infection in some degree at least, for it is a foreign body in the wound, and it provides a channel of communication between the wound and the outer world.

#### STEP 9. THE DRESSING

The application of the operative dressing is as important as the dissection itself, and must not be left to an assistant who is unfamiliar with its details. Our aim is to apply pressure which will obliterate the dead space in the axilla, hold the graft in contact with the chest wall, and immobilize the arm, shoulder,

and chest as much as possible for forty-eight hours. We use fluffed gauze to obtain the pressure, packing it gently into the axilla in between the chest wall and the arm, and over the chest wall, until the surface is flat. We have tried other materials for this purpose but none equals fluffed gauze. The forearm is laid across the upper abdomen, encased in a thick layer of cotton. Two six-inch ACE bandages are then applied around the chest and arm, and securely fastened with safety pins.

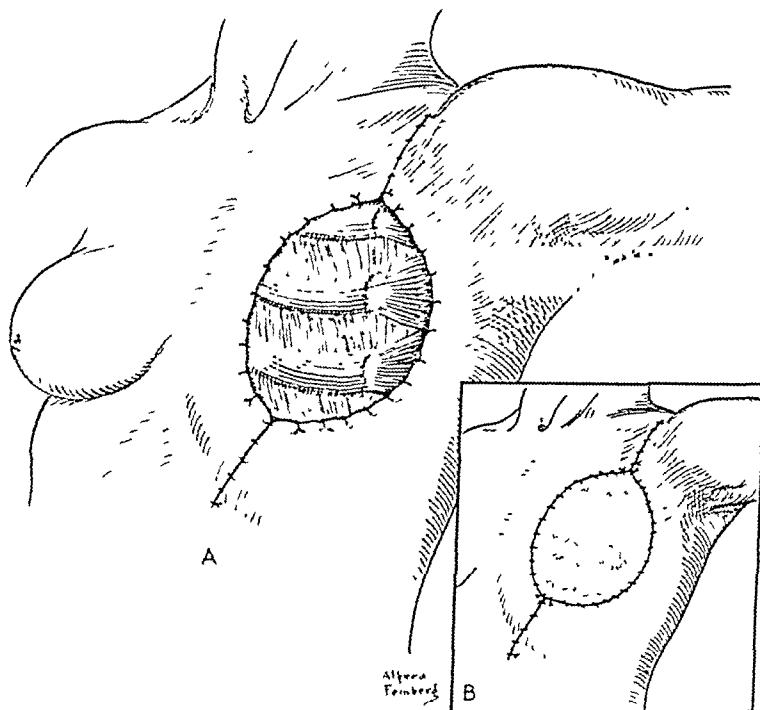


Fig. 23.—The closure of the wound.

### SHOCK

The experienced operator, working steadily and rapidly, can complete this operation in five hours. A less experienced surgeon will require an additional hour. Unless precautions are taken to avoid it, shock will usually develop after this length of time. The most important of these precautions is careful hemostasis. After a little familiarity with the special anatomy of the region the surgeon can identify and clamp almost all of the vessels before cutting them. We use silk throughout the operation and it is our impression that its use favors good hemostasis. As compared with catgut, silk is a finer and more pliable ligature material, and the surgeon using it develops a sense of precision and delicacy which enables him to tie small vessels accurately.

Gentle handling of the tissues is also important. The late George Crile put it well many years ago when he classified surgeons as the carnivorous type who stretch, tear, and crush the tissues, and the herbivorous type who dissect gently.

In operations like the one we have been describing where a large area is denuded, drying of the tissues must be guarded against for it, too, causes shock. We keep all of the wound, except the small area in which we are dissecting, covered with moist towels or compresses. It is not possible to indicate in the drawings, which we have included to illustrate the steps of our operation, the degree to which we keep the tissues covered, but we hope the reader will understand that it is our constant care.

It is usually desirable to guard against the development of shock by giving an intravenous infusion of normal saline solution during the last part of the operation. One thousand cubic centimeters, run in slowly, is ordinarily sufficient. If shock nevertheless develops, we give whole blood promptly, but it is not often that it is needed. The blood pressure, after its initial fall due to the depressive effect of the avertin, usually maintains a remarkably even level if the precautions which we have described are followed.

#### THE AFTERCARE

Rest for the wound and early resumption of fluid and food intake are the immediate objectives of the aftercare. Rest for a wound of the chest wall can be only relative, of course, because of the respiratory movement, but it is of benefit to keep the patient on her back without turning for the first forty-eight hours. This position is tedious, but since we use morphine generously during this period, patients usually tolerate it.

At the end of forty-eight hours we remove the ACE bandages and the fluffed gauze, but we do not disturb the xeroform gauze covering the skin graft. There is no longer any need of a pressure dressing and we cover the wound merely with several layers of gauze fastened with a frame of adhesive around its edges.

On the sixth or seventh day we take down the dressing completely for the first time, removing the sutures around the graft and trimming its overlapping edge. It is wise to leave in place a few of the sutures which fix the flaps to the chest wall, as well as alternate ones along the suture line of the flaps, for a few additional days.

Our patients are ordinarily out of bed on the seventh postoperative day and home on the fourteenth day. The donor area on the thigh, also covered originally with xeroform gauze, is not ordinarily dressed until the day of discharge, when it will be found to be healed.

Some special attention must be given to arm function. After the compression dressing has been removed and the arm freed forty-eight hours postoperatively, we urge the patient to use her arm for all its usual functions, such as eating and writing, except those which require marked abduction. By the seventh or eighth day postoperatively the axillary flap is usually well adhered to the chest wall and from that time on we urge the patient to increase abduction gradually. During the month that follows, almost the full range of arm motion should be regained. In achieving it, patients have to bear some discomfort, but this is not greater than most will tolerate. The objection occasionally raised that the Halsted operation cripples the arm is incorrect. Pa-

tients who cooperate are eventually able to use the arm for everything from scrubbing floors to playing golf. Fig. 24 shows the absence of any constricting band across the axilla in one of our own patients.

Edema of the arm has always been a hazard of radical mastectomy. We believe that its cause is probably a low-grade sclerosing infection in the axilla. Careful obliteration of the axillary dead space, thus minimizing the accumulation of serum and the opportunity for infection, is the best preventive measure if this theory is correct. Our own experience, at least, confirms it, for we have little trouble with edema. A slight degree has developed occasionally, but marked edema has been rare.



Fig. 24.—Arm motion following radical mastectomy.

The Halsted radical mastectomy has not achieved much popularity in this country, or indeed anywhere in the world, during the half century since the operation was first done. Its performance demands patience and fortitude, but we trust that surgeons do not avoid it on this account. It is our hope that the operation has not been popular because it has been but little known, and our purpose in describing it here in detail has been to interest surgeons in it. Properly performed, the operation is safe, and gives a satisfactory functional result. And its truly radical character as compared with the usual so-called radical mastectomy gives an edge of advantage over that formidable opponent, mammary carcinoma.

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# THE TREATMENT OF INOPERABLE CARCINOMA OF THE BREAST WITH IRRADIATION

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**M**OST experienced radiotherapists are enthusiastic about the good results obtained with radical surgery in early cancer of the breast, but less than one-fourth of the patients entering cancer clinics today can hope for a surgical cure. This statement is well borne out by the carefully compiled statistics of Haagensen and Stout<sup>1</sup> who recently reported a series of 1,040 patients with mammary cancer seen at the Presbyterian Hospital in New York from 1915 to 1934. Of this group 640 were treated by radical mastectomy and 231, or 22.2 per cent of the total number, were classed as five-year clinical cures. This means that 809, or 77.8 per cent of the total number, finally succumbed to the disease and required some form of palliative therapy during the final years of their lives.

Daland<sup>2</sup> has shown that the average duration of life in untreated cancer of the breast is 40.5 months from the time of observation of the first symptoms, while 40 per cent of the patients are alive at the end of three years, 22 per cent at the end of five years, 9 per cent at the end of seven years, and 5 per cent at the end of ten years. These figures indicate that in actual practice the effort expended in the care of incurable mammary cancer completely overshadows the purely surgical phase of the subject and yet the surgeons have written so prolifically about their side of the picture that the general physician who loses all interest when surgery fails is hardly to be blamed for his attitude.

Certainly more should be written about the palliative treatment of cancer, a field in which the radiologist now plays a major role. Pack<sup>3</sup> has recently criticized the existent attitude of both the laity and the profession toward this important subject. The properly treated patient with incurable cancer of the breast often has a life expectancy of from three to ten years, a great portion of which may be lived in comfort. As Pack pointed out, the diagnosis of such incurable diseases as arteriosclerosis, chronic nephritis, diabetes mellitus, and coronary disease is accepted with equanimity, fortitude, and optimism by most patients, whereas the term cancer tends to induce deep mental depression in both the patient and the attending physician.

## SELECTION OF CASES

Tumor clinics have found it extremely difficult to formulate plans of procedure designed to give each cancer patient the best available treatment. Although radical mastectomies have been done for more than fifty years, scientifically sound indications for the operation have crystallized very slowly. Every radiologist who has taken care of postoperative mammary cancer has been impressed with the obvious harm done by surgery in certain instances and Haagen-

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sen and Stout have recently produced definite confirmation of this impression. Their studies have produced data which now make it possible for the physician to decide whether a patient with carcinoma of the breast should be subjected to surgery or receive only palliative therapy. They stated, "Women of all age groups who are in good enough general condition to run the risk of major surgery should be treated by radical mastectomy except as follows: (1) when the carcinoma is one which developed during pregnancy or lactation; (2) when extensive edema of the skin over the breast is present; (3) when satellite nodules are present in the skin over the breast; (4) when intercostal or parasternal tumor nodules are present; (5) when there is edema of the arm; (6) when proved supraclavicular metastases are present; (7) when the carcinoma is the inflammatory type; (8) when distant metastases are demonstrated; (9) when any two or more of the following signs of locally advanced carcinoma are present: (a) ulceration of the skin; (b) edema of the skin of limited extent (less than one-third of the skin over the breast involved); (c) fixation of the tumor to the chest wall; (d) axillary lymph nodes measuring 2.5 cm. or more in transverse diameter and proved to contain metastases by biopsy; (e) fixation of axillary lymph nodes to the skin or the deep structures of the axilla and proved to contain metastases by biopsy."

#### METHODS OF TREATMENT

In 1932 Adair<sup>4</sup> summarized the various procedures used successfully in the palliative care of advanced cancer of the breast. In addition to irradiation therapy he listed palliative surgery for the removal of sloughing, necrotic tissue, and local recurrences; electrocoagulation for the removal of small skin recurrences; medication for anemia, anorexia, sleep, relief of pain, and bone repair; special surgical procedures for the relief of lymphedema of the arm; plaster of Paris jackets and casts for fractures, and cordotomy for the relief of severe pain. In addition to all of these things the cancer patient derives an unbelievable amount of good from a cheerful and hopeful attitude assumed by her physician whether he be a surgeon or a radiologist. The improvement in morale becomes apparent early when a woman who has been told that she has a hopeless condition enters a clinic where numerous things are done for her by a physician who inspires confidence.

The radiologist has a number of helpful methods at his command. Although some clinics use radon seeds for interstitial therapy, we favor the weak radium needles advocated by Keynes.<sup>5</sup> These needles produce a minimum of sloughing and fibrosis and their careful use will often completely eradicate both primary and secondary malignant tumors in and about the breast. Although we do not believe that they should be given preference over radical surgery when it can be done, they become very useful in those cases in which the more radical procedures are contraindicated.

In our clinic, needles having active lengths of 2.0 and 4.0 cm. and wall thicknesses of 0.6 mm. of platinum are used. All of the needles contain approximately 0.6 mg. of radium per cm. of active length and they are placed approximately 1.0 cm. apart in layers within or beneath the tumor to be treated for a

period of seven days. The methods of implanting the needles and calculating dosage have been described in previous articles.<sup>6, 7</sup> Some have advocated the use of large numbers of these needles applied externally to the chest wall by means of a radioactive jacket, but this method is uneconomical and has been followed by rib damage in enough cases to render its value somewhat doubtful.

Radiotherapists have attempted actually to cure malignant tumors of the breast with x-rays for many years, using one technical variation after another. Although these tumors may partially or completely disappear, they are seldom permanently controlled when the doses used are safe for the normal tissues. Unfortunately, the fat overlying and incorporated in the breast and the pulmonary structures lying immediately beneath it are seriously damaged by curative doses, particularly when areas large enough to include the original growth and its lymphatic extensions are irradiated. The alveolar structures in the lungs are especially sensitive to x-rays and the type of damage produced has been carefully studied by Groover, Christie, and Merritt,<sup>8</sup> McIntosh and Spitz,<sup>9</sup> Freid and Goldberg,<sup>10</sup> Warren and Spencer,<sup>11</sup> Jacobson,<sup>12</sup> and Leach, Farrow, Foote, and Wawro.<sup>13</sup> Even with a divided dose technique which tends to spare normal structures, Leach, Farrow, Foote, and Wawro observed many cases of pulmonary fibrosis in which the lung received approximately 5.0 T.E.D., and in some instances the irradiation reaching the lung amounted to only 2.5 T.E.D. Since 5.0 T.E.D. is well below the curative dose the limiting factor of pulmonary fibrosis becomes evident.

In treating breast tumors the x-ray beams are always directed tangentially to the chest wall in an effort to diminish lung damage but efficient irradiation of the deep lymphatics of the chest wall and axilla must include some of the pulmonary structures.

A patient can survive even when an entire lung is fibrosed, but elevation of the dosage above safe limits for the pulmonary structures frequently produces a radiation osteitis in the ribs and pathologic fractures may occur. Paul and Pohle<sup>14</sup> have recently described fifteen such cases.

Pulmonary fibrosis, severe skin reactions, and irradiation osteitis produce very unpleasant symptoms. Palliative x-ray therapy should, therefore, be given with techniques which reduce these sequelae to a minimum.

In the beginning single massive doses of x-rays were administered to each area treated, and moderate voltage and filtration were used in an effort to deliver a relatively large dose to the chest wall and breast and a relatively small dose to the underlying lung. Large doses were delivered to breast tumors by crossfiring them through a number of areas. This method is still used at the Mayo Clinic, and MacCarty and Leddy<sup>15</sup> report satisfactory regression of ulcerating carcinoma of the breast treated through four to six sectors at one sitting. The factors used are: 130 kv.; a target skin distance of 40 cm.; a tube current of 6.0 Ma.; a filter of 6.0 mm. of aluminum, and a dose per area of 500 to 600 roentgens. (All x-ray doses noted in this paper are given in roentgens measured in air.)

Many metastatic lesions cannot be efficiently crossfired and a single dose of 600-roentgens given through one skin area is not large enough to produce the

best results. In 1932 Coutard<sup>16</sup> first reported the French divided dose method in the American literature. He showed that doses large enough to damage cancer cells severely could be given safely through a single area when only a fraction of the total dose was given each day. Coutard originally treated carcinoma of the larynx and pharynx situated several centimeters below the skin surface and it seemed logical to apply his technique to cancer of the breast located at a similar depth. In 1933 such a plan was adopted at the Memorial Hospital in New York and in 1935 some of the results were reported by Adair.<sup>17</sup> He observed a complete microscopic disappearance of carcinoma in 33 per cent of the breasts in which 1,800 roentgens were applied to each of two portals laid out so as to crossfire the tumor, and a similar result in 22 per cent of the metastatic axillary lymph nodes crossfired in the same manner through three portals. This work was done with 200 kv. equipment and each area received not more than 300 roentgens per day. Adair did not use more than 1,800 roentgens per area because his work was done on patients with operable cancer and he wished to keep the normal tissues in good condition for operation.

Patients with inoperable cancer can be given larger doses and in our clinic 15 cm. portals are treated with 2,100 to 2,400 roentgens at the rate of 300 roentgens daily. Smaller areas may be treated even more intensively with safety.

The value of castration in the care of advanced mammary cancer was first established in 1896 when Beatson<sup>18</sup> reported improvement following surgical removal of the ovaries in three cases. Other surgeons have reported improvement in approximately 25 per cent of the patients treated by surgical castration and Foveau de Courmelles<sup>19</sup> described the first good results obtained with irradiation castration in 1909. The method is most useful when bone metastases are present and should always be tried when a patient with inoperable cancer has not reached the menopause. In our clinic the artificial menopause is produced by applying 600 roentgens to each of four 15 cm. portals, treating one area per day for four successive days. Two areas are laid out over the front and two over the back of the pelvis. The factors are: 200 kv., a target skin distance of 50 cm., a tube current of 25 Ma., and a filter of 0.5 mm. of copper and 1.0 mm. of aluminum. The menopause should be fully established about six weeks after the completion of this therapy.

#### IRRADIATION SICKNESS

The administration of large doses of x-rays usually produces a syndrome characterized by anorexia, malaise, nausea, and vomiting. The severity of the symptoms depends upon the size of the daily dose, the size of the area treated, and particularly upon the portion of the body irradiated. The most severe reactions are produced by treatment of the upper abdomen. Thirteen theories covering the mechanism producing this condition are listed in a previous article,<sup>20</sup> but the exact cause of the symptom complex is still poorly understood.

Drugs capable of depressing the vomiting center are very helpful in relieving the nausea and vomiting. In our early work we used chloral hydrate and sodium bromide with some success, but in more recent years the barbit-

urates have proved more valuable. Nembutal has been recommended by Richards and Peters<sup>21</sup> and Popp,<sup>22</sup> and a 3 gr. nembutal suppository will usually produce marked relief. The intravenous injection of salt solution and glucose has also produced amelioration of the symptoms and the administration of one or two liters of 5 per cent glucose in a normal saline solution should be used when nausea and vomiting persist.

Many attempts have been made to perfect a preventive form of medication which might be given the ambulatory patient before and during the period of irradiation. In 1933 Dietel<sup>23</sup> reported good results obtained with liver extract and Webster<sup>24</sup> and Young<sup>25</sup> substantiated his findings. These reports pointed to vitamin imbalance as a possible underlying cause of treatment sickness and a series of experiments<sup>26</sup> carried out at the Baylor Medical School in 1937 seemed to indicate that animals could be partially protected against roentgen intoxication by vitamin B<sub>1</sub>. After trying various combinations it is now our belief that the entire B complex gives some protection against the milder forms of irradiation sickness and that it is better than any one of its component parts.

Before a long series of x-ray treatments is started the patient is asked to take a capsule after each meal containing 1 mg. of thiamine chloride, 0.333 mg. of riboflavin, 200  $\mu$ g. of pyridoxine hydrochloride, 2.0 mg. of nicotinic acid, and 250  $\mu$ g. of pantothenic acid. When possible, a daily intramuscular injection of 1.0 c.c. of liver extract containing 2.0 U.S.P. units is also given. If the patient's condition is poor or if nausea and vomiting appear, the oral vitamin therapy is replaced by a daily intravenous injection of 2.0 c.c. of a solution containing 10 mg. of thiamine chloride, 4.0 mg. of riboflavin, 150 mg. of nicotinamide, 10 mg. of pyridoxine hydrochloride, and 5 mg. of pantothenic acid. This type of medication not only offsets the effect of the irradiation but it tends to improve the patient's appetite and general health as well.

The successful use of large doses of pyridoxine hydrochloride in controlling the nausea and vomiting of pregnancy was reported by Willis, Winn, Morris, Newsom, and Massey<sup>27</sup> in 1942. This work, done at the Baylor Medical School, has been substantiated by Weinstein, Mitchell, and Sustental<sup>28</sup> and suggests a specific effect of vitamin B<sub>6</sub> on nausea of toxic origin. We hope to have data in the near future on the use of this drug in the treatment of irradiation sickness.

#### LESIONS TREATED

*Large Tumors in the Breast in Incurable Cases.*—When large masses of malignant tissue have become necrotic and are producing a foul odor, surgical resection offers quick symptomatic relief. However, these large tumors often show marked shrinkage following radiation. When an infected ulcer has appeared in a large tumor the use of activated zinc peroxide paste for several days prior to irradiation is a helpful procedure. The multiple single dose method given through four to six sectors is quite satisfactory but most radiologists prefer to crossfire the tumor through two or three portals, using a

divided-dose tangential technique with 200 kv. equipment. Each portal may be given 2,100 to 2,400 roentgens at the rate of 300 roentgens per day to each area. This type of therapy produces a marked skin erythema in eight to ten days followed by desquamation and tanning. When this reaction is at its height the patient complains of some burning and itching and obtains much relief from the free use of a wash containing 1.0 gr. of phenol, 2.0 dr. of glycerine, 4.0 dr. of zinc oxide, and 6.0 ounces of limewater. In certain locations portions of the treated skin may be temporarily denuded. When the skin surface is lost the wash should be replaced by a soothing ointment. Boric acid or nupercainal ointment usually gives relief. Tumor regression becomes apparent in about three weeks after the treatment is finished and may continue for another three to six weeks.

*Involvement of the Skin.*—This complication may manifest itself as a puckering of the skin, a reddened thickened-area nodule formation, or cancer en cuirasse. As O'Brien<sup>29</sup> has pointed out, the appearance of skin metastases is almost always a very bad prognostic sign and a cure is rarely obtained. Occasionally radical treatment of a small single recurrent nodule is successful but the common surgical practice of removing one recurrence after another from the skin and subcutaneous tissues has little to commend it. Adair<sup>30</sup> stated that since "surgery fails in a larger proportion than heavy irradiation, it is best to treat a definite region of recurrence with a sufficiently large portal to more than cover it, employing about 200 r to 250 r daily, up to approximately 4,000 r total." Although he advocated a voltage of 200 kv., Fried and Goldberg<sup>31</sup> used a somewhat lower dosage with low or intermediate voltage in an effort to spare the pulmonary tissues. We prefer implanted low intensity radium needles for such lesions because a curative dose can be safely administered without damaging the intrathoracic structures.

When multiple nodules or cancer en cuirasse appear, no type of treatment will cure the patient and only palliative therapy is indicated. Prolonged improvement often follows the use of divided doses of x-rays generated at 200 kv. The entire anterior chest wall should be divided into 15 cm. squares, 1,800 to 2,100 roentgens being administered to each at the rate of 300 roentgens per day. This therapy may be repeated after six to eight months, if necessary, and the skin lesions can in most instances be fairly well controlled until internal metastases appear.

Parasternal masses which are attached to the chest wall and may or may not ulcerate through the skin may be completely eradicated with irradiation therapy. Adair reported ten such cases successfully treated with 15,000 mc. hr., given by means of a radium pack and followed by a single massive dose of high voltage x-rays. We use weak radium needles for these lesions and all others where it is desirable to give a large dose to an accessible tumor.

*Metastases in Axillary Lymph Nodes.*—Enlarged axillary glands containing carcinoma are found following operation when the nodes apparently were too deep for complete extirpation and in advanced cases which are beyond

surgical aid. A swollen arm on the affected side is often produced by the pressure of such glands on the return circulation. However, in some cases the lymphedema results from operative procedures or from the fibrosis produced by intensive irradiation.

For some reason which is not understood, cancer cells growing in lymph nodes are more resistant to irradiation therapy than the malignant cells found in the primary tumor. Axillary fat stands heavy irradiation very poorly and although a combination of interstitial radium and a crossfire x-ray technique sometimes produces complete regression of cancer in axillary nodes, the resulting reaction is not justified in incurable cases. When implanted radium needles or radon seeds are used, great care must be exercised to space the sources so that an excessive dose will not reach the brachial plexus. Such a mishap produces intractable excruciating constant pain which is to be avoided even though the response to treatment is satisfactory.

Duffy and Lucas<sup>32</sup> have estimated the dosage delivered to the depths of the axilla with external x-ray therapy administered through two, three, four, and five portals. With 200 kv. equipment and three portals, the dose reaching the deeper glands amounts to 200 per cent of that given each area. Anterior and posterior portals measure 10 by 10 cm. and a third area on top of the shoulder measures 10 by 8 cm. When each portal receives a total of 2,100 roentgens given by the divided-dose technique, the palliative results are usually good and in some instances similar doses given to 15 by 15 cm. areas laid out over the front and back of the axilla suffice.

*Metastases in Supraclavicular Lymph Nodes.*—(Careful palpation may reveal small metastatic nodes just behind the inner end of the clavicle or just behind the mid-portion of the bone. Since this finding renders the patient incurable its detection is most important. In later stages of the disease multiple glands appear extending from the mastoid to the clavicle. Deep-seated nodes below the mastoid may produce pain about the ear and edema of the face.

Carcinomatous invasion of the brachial plexus constitutes one of the most difficult problems encountered. Pain in the arm is so intense that morphine does not give relief and the muscles of the hand show marked atrophy. The patient is thoroughly exhausted from loss of sleep and the condition is indeed pitiful. Irradiation produces no improvement and a high cordotomy offers the only hope of relief.

Although Adair has reported the control of isolated supraclavicular nodes with very heroic external irradiation, his results necessitated severe damage to the skin, subcutaneous tissues, and clavicle. In our experience single nodes are best treated with implanted radium needles of the Keynes type. Although the skin over the implanted area develops atrophy and telangiectasia, the damaged region is localized and produces no untoward symptoms. Supraclavicular nodes have remained quiescent for three to six years following this procedure.

Larger areas must be treated with external irradiation and the neck does not lend itself well to a crossfire technique. For this reason the divided-dose

method must be used over single portals. The skin of the base of the neck is easily damaged with x-rays and the total dose used rarely exceeds 2,100 roentgens. When this type of therapy is directed toward the midline, a rather severe reaction is produced in the mucosa of the esophagus. In six or seven days after the treatment is finished the patient complains of soreness and difficulty in swallowing, but these symptoms subside after seven or eight days and no permanent injury results. It is sometimes necessary to use only soft and liquid food during the reaction stage and cold foods such as ice cream are well tolerated. Acetyl salicylic acid or one of the nupercaine preparations may be dissolved in the mouth and swallowed slowly before each meal for relief of discomfort.

*Skeletal Metastases.*—Osseous metastases from mammary cancer may appear in practically every bone in the skeleton. Lenz and Freid<sup>33</sup> have made a painstaking study of eighty-one such cases. In only six did roentgenographic or clinical evidence of other metastases precede skeletal invasion. The regions most frequently involved were the pelvis, spine, and femurs. The first symptoms were usually pain and pressure tenderness and in 75 per cent of these patients the examiner's attention was drawn to the bone metastases because of the complaint of localized pain. In nine cases the complaint of pain preceded the roentgenographic demonstration of the lesions by one-half to twelve months. Pathologic fracture was observed in twenty-one cases and this complication often occurred before the skeletal invasion became widespread.

In the roentgenogram two types of metastases are observed. One, which is likely to become widespread, is characterized by a diffuse moth-eaten appearance, while in the other localized areas of complete bone destruction with sharply defined margins are seen. Many involved vertebral bodies collapse early producing various stages of kyphosis and in some instances a transverse myelitis from pressure on the spinal cord.

The radiotherapist dealing with this complication is doubly blessed because he has at his command two methods of treatment capable of producing good results. It has been known for years that relatively small doses of x-rays delivered directly to bone metastases of mammary origin often relieve pain and may even produce a recalcification of the destroyed osseous structures. In 1931 Daland<sup>34</sup> reported striking improvement of generalized metastatic bone lesions in a patient subjected to x-ray castration and in 1933 similar results were obtained in our clinic. In 1936 Dresser<sup>35</sup> published a careful study of thirty women afflicted with skeletal metastases treated by x-ray castration alone. Of this group 43.3 per cent obtained relief of pain, 30 per cent showed regression of the lesions, and only 26.6 per cent showed no response to treatment. No improvement was observed following ovarian irradiation in any woman past the menopause. In 1936 we<sup>36</sup> reported a small series of cases in which the two methods were combined. In this experience very few patients who have not reached the menopause fail to obtain relief of pain from this plan of treatment. The patient first receives four massive doses of x-rays over the pelvis to produce an artificial menopause as previously described. Each metastatic



area is then crossfired through two or more 15 by 15 cm. portals, a dose of 600 roentgens being delivered to a single portal each day. This entire procedure can be carried out in a reasonable period of time even when multiple bone metastases are present. Relief of pain begins in two or three weeks after the series is finished and the maximum improvement appears in six to eight weeks. Most patients treated in this manner show a gain in weight of fifteen to twenty pounds and a general improvement in their appearance which is most striking. Unfortunately, the good results are not permanent but often last from one to three years. When bone pain reappears it can frequently be relieved a second time by repeating the local treatment.

Pathologic fractures are serious complications but their treatment is not necessarily hopeless. In many instances healing occurs when the treatment detailed here is combined with immobilization usually produced by means of a plaster cast. The x-ray therapy can be administered through windows cut in the cast and good union has appeared after the completion of the irradiation therapy. Adair and Freid and Goldberg advocated the use of the divided-dose technique in such cases and gave as much as 1,800 roentgens per area. Even compression fractures of vertebral bodies may show a good response if a plaster jacket can be put on early while traction is applied. Adair reported a return of sphincter control in both the rectum and bladder following such treatment used soon after the appearance of the symptoms of transverse myelitis.

*Brain Metastases.*—Intracranial metastases from carcinoma of the breast are relatively common in the last stages of the disease. Freid and Goldberg observed clinical evidence of such lesions in 20 per cent of 369 advanced cases. There was roentgenologic evidence of skull invasion in 61 per cent of this group, and direct extension from the metastases in the calvarium was demonstrated at autopsy in seven cases. Involvement of the pituitary occurred in four cases and of the pineal gland in two cases. Cerebral metastases found at post-mortem examination in five cases produced no symptoms during life. When the pituitary lesions were large enough to produce symptoms a typical diabetes insipidus was produced. The longest survival period after the discovery of cerebral involvement was thirty-two months. Localizing signs appeared without increased intracranial pressure in twenty-nine patients and were accompanied by such an increase in thirty patients. In nine the only symptoms were those of gradually increasing pressure. In our practice we have observed sixth nerve involvement as the first sign of brain invasion on so many occasions that we are constantly on the lookout for early strabismus.

Some neurological surgeons advocate the removal of brain lesions when other parts of the body are relatively free of metastases. However, the palliative results with irradiation are usually so good that this radical procedure seems unjustified. Relief of symptoms lasting from six months to two years has been observed and the treatment can oftentimes be successfully repeated.

It is our custom to crossfire the affected portion of the brain through two or three portals when localization is possible. In other cases the skull is treated

through four triangular portals covering the entire cranial vault. Each area receives a daily dose of 300 roentgens and a total dose of 1,800 roentgens, but only one area is treated per day. In some instances irradiation produces an increased intracranial pressure sufficient to require treatment but this complication is rarely troublesome. All of the hair falls out soon after the series is finished but it usually grows again after four to six months. In women an attempt is made to shield the top of the head so that the hair remaining in this region can be made to cover the bald spots, but in the more advanced cases this is not possible. Some patients wear wrap-around turbans with a small amount of hair attached to the edges so arranged as to conceal completely the absence of hair on the head.

*Spinal Cord Metastases.*—The symptoms of spinal cord pressure usually result from lesions growing from the vertebral bodies but occasionally the metastases are within the neural canal. In the series studied by Freid and Goldberg, invasion of the dura occurred in four cases and of the cord itself in two cases. Treatment of the type used for brain metastases is frequently effective if it is applied before permanent damage occurs. The rays are directed at the cord lesion through two to four portals depending upon its depth below the surface.

*Intrathoracic Metastases.*—Figures covering the incidence of intrathoracic metastases in patients dying of mammary cancer, published by different pathologists, show a marked variation but the discovery of this complication in 89 per cent of the post-mortem examinations reported by Freid and Goldberg indicates that a careful search will reveal some involvement of this region in almost every fatal case. The first extension may appear in the lungs, pleura, mediastinal nodes, heart, or pericardium, but as the disease progresses two or more of these structures usually are invaded. Combined invasion of the lungs, pleura, and mediastinal nodes is the commonest finding.

Since early lesions are often asymptomatic, an x-ray examination of the chest is one of the first steps in the examination of every patient. The smaller metastases, particularly those in lymph nodes, cannot be demonstrated and for that reason a routine roentgenogram of the chest should be made every two months.

The findings in the lung fields are of three varieties. Rounded, sharply defined, translucent areas of increased density are pathognomonic. However, in some cases the metastases appear as irregular dense areas with poorly defined borders of the type seen with disseminated tuberculosis, while in others a stranded invasive process extends into the lung fields from the hilus. Pleural involvement produces all of the roentgen-ray signs observed with pleurises of infectious origin and cannot be differentiated from them when the history is not available.

The earliest symptom is a nonproductive cough. As the intrathoracic lesions grow, dyspnea becomes a troublesome symptom and pain and tenderness in the chest usually indicate pleural invasion. Hoarseness from vocal cord paralysis and swelling of the neck secondary to pressure on the superior vena cava may follow enlargement of mediastinal lymph nodes.

On the whole, the treatment of intrathoracic lesions with roentgen rays is unsatisfactory. This is partially due to the fact that the patient is likely to be suffering from generalized carcinomatosis by the time intrathoracic metastases are well established. A localized pleurisy sometimes regresses after intensive irradiation therapy. However, we have seen pleurisy with effusion in cancer disappear without treatment and one cannot be certain that this complication is always of malignant origin. In the absence of pulmonary lesions, a crossfire technique applied to a pleurisy at one base is justified.

Generalized pulmonary metastases should never be irradiated because of the serious changes produced in the lungs by efficient dosage. Occasionally it seems worth while to treat a single nodule when the patient is in good condition and other metastases are not demonstrable. Moderate doses may also be directed at the mediastinum with some temporary success when pressure symptoms from enlarged glands produce severe distress.

As a rule better palliative results are obtained when irradiation of the thorax is omitted. The cough and discomfort are best controlled with mixtures containing codeine or morphine to which small amounts of one of the barbiturates are added. When pleural effusions appear paracentesis often relieves the resulting dyspnea.

*Intra-abdominal Metastases.*—Abdominal extension indicates a generalized dissemination of the disease in mammary carcinoma and no efficient method of retarding this dissemination is now available. Autopsy findings indicate that all of the viscera as well as the mesenteric and retroperitoneal lymph nodes and peritoneal surfaces may contain implants. The organs most commonly involved are the liver, adrenals, ovary, spleen, and kidney.

In most advanced cases the liver contains one or more metastatic nodules and shows some degree of enlargement. The nodules may compress the hepatic ducts and produce a marked jaundice. These changes give rise to a chronic indigestion characterized by epigastric fullness after eating, eructations, nausea, and vomiting. Persistent gastric symptoms in a patient with cancer of the breast always render the prognosis poor even though the liver is not palpable.

Constant abdominal pain may be due to a large, tender liver, marked ascites, or enlarged para-aortic and mesenteric lymph nodes. In some instances the pain resembles that produced by peptic ulcer or gastric cancer. The appearance of abdominal invasion is soon followed by weakness, cachexia, loss of weight, and a great variety of lesser symptoms.

Although some radiologists advocate irradiation therapy over the abdomen, particularly when the liver is enlarged, we believe that the questionable improvement obtained in no way offsets the objectionable symptoms of irradiation sickness which invariably follow this form of treatment. Patients with abdominal metastases are best handled by the internist who does an abdominal paracentesis when it is indicated and makes the victim's last days as comfortable as possible.

The following case histories illustrate some of the points covered in the paper and show that a patient may live for a number of years in relative comfort after the diagnosis of incurable mammary cancer is made.

CASE 1.—In 1933 a tumor was removed from the right breast of Mrs. F. C. B., who was then 35 years of age. The operation was done by her home physician who told her that the tumor was not malignant. In October, 1934, she visited a clinic in another city where a radical resection of the right breast was carried out. Adenocarcinoma, grade III, was found in multiple nodules in the breast and in two axillary lymph nodes. She received postoperative x-ray therapy over the chest and axilla in the same clinic. This treatment was repeated in 1935.

In 1937 she returned to the same clinic for surgical removal of a supraclavicular lymph node which contained adenocarcinoma. Following this operation x-ray therapy was given over both sides of the neck and the right axilla.

In February, 1941, the same physician removed a gland measuring 2.0 cm. in diameter from the left axilla and it also contained adenocarcinoma. This operation was followed by short series of x-ray treatments given in March, April, and July in 1941, and in November, 1942. At her last visit for x-ray therapy she complained of loss of vision. She could only detect light with the right eye but could see fairly well with the left eye. X-ray examinations of the skull, chest, and spine revealed no evidence of metastases.

She entered the clinic in January, 1943, just ten years after the onset of her illness complaining of headache, nausea, vomiting, a staggering gait, and complete loss of vision in the right eye. Examination revealed a small metastatic node in the left axilla but no other external evidence of carcinoma. Roentgenograms of the skull, chest, and spine revealed no evidence of metastases.

From Jan. 23, 1943, to Feb. 12, 1943, she received a daily dose of 315 roentgens delivered to three 10 by 15 cm. portals laid out over the occipital and both parietal regions. The areas were treated in rotation until each one received 1,890 roentgens and only one area was treated each day. The factors used were: 220 kv.; 20 Ma.; a target skin distance of 50 cm.; and a filter of 0.8 mm. of tin, 0.25 mm. of copper, and 1.0 mm. of aluminum.

She improved slowly and on March 30, 1943, was free of headache and vomiting and could walk without difficulty. The vision did not improve in the right eye. From March 30, 1943, to April 6, 1943, a total of 1,890 roentgens was administered to the left axilla using the same factors.

On Dec. 15, 1943, she returned complaining of pain in the right lumbar region, hip, and leg. Although x-ray examination showed no bone metastases, castration seemed to be indicated. On four successive days she was given 600 roentgens to each of four 15 by 15 cm. portals laid out over the front and back of the pelvis. The treatment factors were 200 kv., 25 Ma., a target skin distance of 50 cm., and a filter of 0.5 mm. of copper and 1.0 mm. of aluminum.

On Jan. 19, 1944, the pain in the lower back was much better but the patient complained of pain in the left shoulder and arm and weakness of the left hand. No evidence of metastases in the cervical spine was revealed by x-ray examination. However, single doses of 600 roentgens were given to 10 by 15 cm. portals over both sides of the neck and the anterior and posterior aspects of the left shoulder, using the same factors as at the last visit.

On March 15, 1944, the pain in the shoulder and arm was completely relieved and she had no new symptoms referable to the brain lesion except slight dimness of vision in the left eye. She also complained of some pain in the calf of the right leg. Single doses of 600 roentgens were delivered to 15 by 15 cm. portals over the anterior and posterior aspects of the right lumbar region and total doses of 1,800 roentgens were given to the lateral aspects of the skull through 15 by 15 cm. portals at the rate of 300 roentgens per day using the factors originally employed in treating the head.

When she left the hospital on March 30, 1944, she was free of pain and the vision in the left eye was improving.

*Comment.*—The progress of this patient illustrates the futility of repeated surgical removal of lymph nodes in an incurable case. The pain in the cervical

and lumbar regions may have been produced by bone metastases. In some instances pain appears months before bone changes can be demonstrated roentgenographically. This patient is rather remarkable in that she is alive with metastases and in fairly good condition eleven years after the appearance of an actively growing carcinoma of the breast.

CASE 2.—Mrs. P. P. entered the clinic in May, 1942, when she was 45 years of age. A hard tumor filled the outer half of the right breast and the overlying skin had an orange-peel appearance. Several small glands were felt high in the right axilla and two similar nodes measuring 1.0 cm. in diameter were felt above the mid-portion of the right clavicle. Roentgenographic examination revealed no evidence of intrathoracic metastases. A clinical diagnosis of inoperable carcinoma of the breast was made without microscopic confirmation.

X-ray therapy was administered over three areas. The breast was crossfired through two 15 by 20 cm. portals. The lateral portal included the axilla. A 15 by 15 cm. portal included the right neck above the clavicle. Daily treatments of 300 roentgens were given to single areas in rotation until each one had received a total of 2,100 roentgens. The treatment factors were 200 kv., 15 Ma., a target skin distance of 50 cm., and a filter of 0.4 mm. of tin, 0.25 mm. of copper, and 1.0 mm. of aluminum.

When the patient returned six weeks later the tumor in the breast was much smaller, the axillary nodes were just palpable, and the supraclavicular nodes could not be felt. The treated areas showed a marked tan and some desquamation.

In September, 1942, she developed a hacking cough with discomfort in the right chest. A roentgenogram revealed a small pleural effusion at the right base. The chest was strapped and she was given sedatives but no irradiation was administered. She returned six weeks later entirely free of symptoms and a roentgenogram showed no evidence of the pleurisy which apparently had an infectious etiology. At that visit the right breast was still somewhat enlarged and a deep mass of fibrosis was felt at the site of the tumor.

In October, 1943, she discovered a movable subcutaneous nodule measuring 0.5 cm. in diameter on the inner aspect of the right arm just above the elbow. A single dose of 640 roentgens was given to a 15 by 15 cm. portal centered over the nodule. The treatment factors were 200 kv., 15 Ma., a target skin distance of 50 cm., and a filter of 0.5 mm. of copper and 1.0 mm. of aluminum. In January, 1944, the subcutaneous nodule had disappeared and she felt perfectly well. The findings in the breast were unchanged and no other evidence of metastases could be found.

*Comment.*—This patient, who undoubtedly had an inoperable carcinoma of the breast, has remained symptom free except for a short attack of pleurisy for two years with x-ray therapy alone. A positive diagnosis could have been made from a supraclavicular node and perhaps one should have been removed for biopsy. Irradiation would have received false credit for relieving a malignant pleurisy if it had been used when the pleural complication occurred.

CASE 3.—Mrs. S. R. entered the clinic in October, 1935, when she was 54 years of age. A physician in a small town had just removed a rather large tumor from the right axilla and a reliable pathologist reported it to be an adenocarcinoma, grade III. About nineteen months prior to this operation a portion of the right breast had been removed without an axillary dissection by the same physician. At the time of admission she was symptom free and no evidence of metastases could be made out either by palpation or x-ray examination.

She received 300 roentgens daily over a 15 by 15 cm. axillary port until 2,700 roentgens had been administered. The treatment factors were 220 kv., 20 Ma., a target skin distance of 50 cm., and a filter of 20 mm. of copper and 1.0 mm. of aluminum.

She did well until November, 1928, when she returned with a hard, flat tumor measuring 4.0 cm. in diameter in the mid-portion of the remainder of the right breast. The overlying skin had an orange-peel appearance. The tumor was crossfired through two 15 by 15 cm. portals at the rate of 300 roentgens per portal per day until each area had received 2,100 roentgens. The treatment factors were 220 kv., 20 Ma., a target skin distance of 50 cm., and a filter of 0.8 mm. of tin, 0.25 mm. of copper, and 1.0 mm. of aluminum.

The tumor in the right breast melted away but in May, 1939, the patient returned with a diffuse swelling of the left breast, the skin of which showed an orange-peel appearance, and a gland measuring 3.5 cm. in diameter in the left axilla. The left breast was crossfired through two 15 by 20 cm. portals. The lateral portal included the axilla and the dosage was exactly the same as that given to the right breast at the previous visit.

All evidence of the disease melted away and she remained well until May, 1941, when she returned with a hard, fixed tumor measuring 2.5 cm. in diameter, growing from the left chest wall just below the inner end of the clavicle. Roentgenograms of the chest wall and lung fields showed no metastases. A dose of 2,100 roentgens was given to a 15 by 15 cm. portal centered over this tumor at the rate of 300 roentgens per day. The tumor disappeared and in June, 1942, a similar series of treatments was given over the right neck because a few enlarged glands had appeared in this region.

In September, 1942, she returned to the clinic looking ill for the first time and complaining of hoarseness and weakness. A roentgenogram of the chest revealed some widening of the aortic arch and a few questionable enlarged mediastinal glands. The tumor in the right breast had recurred and measured 5.0 cm. in diameter. Because of her rather poor condition only a short series of massive doses was given. Four 15 by 15 cm. portals laid out over the mediastinum received 600 roentgens on successive days and the breast tumor was crossfired through two areas of similar size with the same dosage.

In December, 1942, she wrote that she had received some benefit from the last treatment and was moving to another city where she would be under the care of another radiologist.

*Comment.*—It is unnecessary to point out the fact that this patient's life might have been saved by radical surgery at the time of the first operation. However, palliative therapy gave her seven years of relative comfort during most of which time she led a normal life.

CASE 4.—Mrs. T. L. F., 45 years of age, entered our clinic in December, 1940, because of a large, foul-smelling, painful mass which filled the left axilla. Three years previous to admission she had consulted a cancer "quack" who applied a caustic paste repeatedly to a tumor of the left breast for a period of four weeks. She stated that the treatment was extremely painful. However, after a period of four months the slough separated and the resulting wound healed, leaving a very large scar on the chest wall. About eighteen months later the tumor began to grow again and extended up into the axilla. Although she was again treated with caustic paste the new lesion did not improve.

At admission the axilla was filled with a black mass of necrotic tissue. When it was cut away a deep ulcer lined with bleeding, friable tissue and measuring 8.0 cm. in diameter was seen in the axillary fossa. Specimens of this tissue were reported as carcinoma simplex, grade IV. Roentgenograms of the chest revealed no evidence of metastases. The wound was packed with activated zinc peroxide for twenty-four hours and thoroughly cleansed with hydrogen peroxide. A group of fourteen long platinum radium needles, each containing 2.4 mg. of radium in 4.0 cm. of active length, were then inserted into the axilla in a conical pattern so as to surround the malignant ulcer and left in place for seven days.

At the end of six weeks she was much more comfortable and the ulcer was about one-half its former size. Its surface was clean and no definite evidence of malignant tissue could be seen. However, when she returned four months later the ulcer was still present

and active malignant tissue was found at its edges. She was then referred to a surgeon who found it possible to do a resection of the axillary tissues and sear on the chest wall. Healing was uneventful and this patient has remained well for three and one-half years since the date of admission.

*Comment.*—This unfortunate woman could undoubtedly have been cured by radical surgery done when the tumor first appeared. Certainly she could have been saved a great deal of suffering. In the opinion of our surgical consultant, an operation would have been hazardous when she was first seen, whereas it was carried out with ease after the wound was cleaned up with irradiation.

CASE 5.—Mrs. S. J., 43 years of age, entered the clinic on July 9, 1943, because of marked swelling and pain in the right arm. About two years previous to admission a radical resection of the right breast was done in a small town for a proved carcinoma and she was given some form of x-ray therapy for a period of four weeks in another city. One year later a number of recurrent skin nodules were removed surgically. They rapidly reappeared and the surgeon then removed a large portion of the involved skin and applied a graft. Soon afterward the arm began to swell.

At the time of admission an indurated mass of tumor tissue extended from the anterior right chest wall well up into the axilla and the right arm was markedly swollen so that its function was almost completely abolished. Three enlarged lymph nodes measuring 1.0 cm. in diameter were felt above the mid-portion of the right clavicle. Roentgenograms of the chest revealed no evidence of metastases. Portals measuring 15 by 15 cm. laid out over the anterior and posterior aspects of the right axilla and over the right side of the neck each received total doses of 2,100 roentgens at the rate of 300 roentgens per day. The treatments were given on successive days and only one area was treated each day. The treatment factors were 200 kv., 15 Ma., a target skin distance of 50 cm., and a filter of 0.4 mm. of tin, 1.0 mm. of copper, and 1.0 mm. of aluminum. Since this patient was still menstruating, a castration dose was then given through four portals using the method previously described.

She showed steady improvement and at the end of two months was free of pain and had gained ten pounds. At that time the swelling in the arm was much reduced. At the end of ten months the general condition was excellent. The arm was still slightly swollen but she could use it freely. A few small nodules could still be palpated in the right axilla and the supraclavicular nodes were just palpable.

*Comment.*—This case shows the futility of attempting to control multiple skin recurrences with radical surgery. It also illustrates the value of irradiation in the treatment of a swollen arm produced by malignant invasion of the axilla.

CASE 6.—Mrs. F. B., 36 years of age, entered the clinic in 1931 in a semihysterical state after being told by her physician that she had only two months to live and that she might break one of her bones at any time. A radical resection of the left breast had been done for carcinoma in 1929. About one and one-half years later she began to lose weight and to complain of indigestion and pain in the chest. She went to a large clinic where x-ray examination revealed metastases in two thoracic vertebrae, several ribs, one clavicle, and both scapulae.

At the time of admission she was moaning with pain. Both arms were locked about her legs which were drawn up under her chin and she could not be relaxed because of a firm conviction that letting her legs down might produce a fracture. After the administration of large doses of barbiturates she was finally straightened out in bed. Castration

doses of x-rays were given over the pelvis on four successive days and single massive doses were given over each portion of the skeleton in which metastases were demonstrated.

The large doses of morphine which she had been taking were rapidly reduced and at the end of three weeks this drug was completely withdrawn. She was told daily that the information obtained from her former physician was incorrect and that her outlook was good.

At the end of six weeks she was almost free of pain, was able to sit up and was complaining of hot flashes. At the end of seven months she had gained a total of forty-two pounds and was able to lead a normal life. She attended social functions in the evenings and looked unusually well. Roentgenograms of the skeleton showed a recalcification of most of the metastatic areas.

At fourteen months single massive doses of x-rays were given over several tender areas in the thorax and lumbar spine. At sixteen months she revisited her original physician who discovered some asymptomatic metastases in the skull. She was much upset when her attention was focused on these lesions and it was necessary to do a complete epilation to restore her mental equilibrium. At two years pain appeared in the left chest and a moderate amount of bloody fluid was aspirated from the pleural cavity. Roentgenograms revealed a soft tissue mass measuring 3.5 cm. in diameter at the periphery of the lower left lung field. No x-ray therapy was given over this region and the pleural process did not progress. At two years and eight months rather severe pain appeared in the lower lumbar region. It was partially relieved by single massive doses of x-rays but she began to lose weight and complained of weakness. At three years and two months from the time of admission she died with multiple metastases in the liver and lungs.

*Comment.*—In our opinion this patient's physician erred in telling her of the seriousness of her condition and in giving her large doses of morphine as her only form of treatment. If x-ray therapy had been started immediately she could have been spared much mental suffering. It is our custom to tell such patients that they are suffering from a form of arthritis which can be treated with x-rays. Since some forms of arthritis are now treated successfully with irradiation many of our patients obtain relief without realizing that a serious complication has appeared.

#### SUMMARY

With the methods of treatment now available more than 75 per cent of all patients with cancer of the breast applying for treatment are incurable and must receive some form of palliative therapy.

Criteria are now available which make it possible to decide whether any given patient should receive radical surgery or only irradiation therapy and other palliative measures.

The care of patients with incurable mammary cancer has become rather complex but the intelligent use of irradiation therapy enables many of them to live three or more years in relative comfort.

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## THE PROBLEM OF LOCAL RECURRENCE AFTER RADICAL MASTECTOMY FOR CARCINOMA

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FOR some years I have been interested in the question of recurrence of breast cancer in the operative field, and I have been distressed by its frequency.

In the development of the present form of treatment, surgeons have, step by step attempted to remove more and more tissue in the neighborhood of the growth. Halsted introduced a radical procedure which is well known and widely followed. In this operation he removed a "large area" of the skin together with the breast, the pectoral muscles, and the axillary contents. I have been unable to find records of measurements of the skin removed for comparison with the Handley technique. Halsted's method also differed from that of Handley in that he did not advocate wide undercutting of the adjacent skin to permit plastic closure. At times I have had the privilege of observing the technique of some of his pupils and, at times, they have not removed more than a five-inch diameter of skin, which left an area that in those instances could have been closed by plastic methods if the operator had so elected. In other cases, I am certain that more than a five-inch diameter of skin was removed, to the maximum that was permissible, and yet of the fifty cases that Halsted reported in his original paper, local recurrence developed in 31.9 per cent.<sup>1</sup>

Handley<sup>2</sup> later propounded the thesis that it was not necessary to excise so much skin because cancer did not spread in the skin but in the subcutaneous tissue. He, therefore, was content to excise a circular diameter of about five inches and then dissect in a peripheral direction in the subcutaneous tissue so as to leave a flap of skin that could be approximated in most instances. In my practice, I fell under his influence and have followed this method in regard to the skin. However, in small breasts with the removal of such a diameter of skin, I have found it necessary to graft skin.

As time passed, I became more and more interested in the question of the correctness of Handley's position and also that of Halsted. In truth, I have never seen definite proof, in pathologic sections, that cancer spreads in the skin lymphatics or in the subcutaneous lymphatics. But from clinical observations, I am inclined to favor Handley's contention. My bias in favor of skin closure when feasible may have influenced this judgment. If so, I might be proved definitely wrong by the results in our clinic and elsewhere.

Generally speaking, our five-year survival results were comparable to those of the other clinics, when the mathematical statistical errors are considered that creep into a report of less than 10,000 cases. We were satisfied that our results were comparable, but then I began to wonder about the significance

<sup>1</sup>Received for publication, April 15, 1945.

of local recurrences. Theoretically, if an operation is correct it should excise all the local cancer in an operable field. But we found that there was a definite incidence of local recurrence in our patients, in whom we had used the Handley technique.

In a study of 238 cases of plastic closure (Handley) that had been followed for a minimum time of five years, and many much longer, we had evidence of 22.6 per cent local recurrence.

It may be contended that 22.6 per cent local recurrence in the 238 cases indicated that our type of radical operation was inadequate. Therefore, as a check on our results, I have compared these results with those from other clinics (Table I).

TABLE I. RESULTS OF RADICAL OPERATION FOR BREAST CANCER

HOSPITAL	LOCAL RECURRENCE		FIVE YEAR FREEDOM	
	NUMBER	PER CENT	NUMBER	PER CENT
The Roosevelt Hospital <sup>3</sup> (New York)				
(Plastic closure)				
Limited to breast	101	11	62	61
Axilla involved	137	43	24	17
The Presbyterian Hospital <sup>4</sup> (New York)				
(Plastic closure and skin graft)				
Limited to breast	237	23	145	61.2
Axilla involved	385	120	81	21
The St. Lukes Hospital <sup>5</sup> (New York)				
(Plastic closure and skin graft)				
Limited to breast	116	8	68	58.6
Axilla involved	244	52	57	23.3
The Henry Ford Hospital <sup>6</sup> (Detroit)				
(Plastic closure and skin graft)				
Limited to breast	97	6		
Axilla involved	149	31		
(Plastic closure)				
Limited to breast	72	4		
Axilla involved	67	18		
(Skin graft)				
Limited to breast	24	2		
Axilla involved	67	18		
Johns Hopkins Hospital <sup>1</sup>				
(Table XXX)				
Plastic closure	116	46		
Thiersch graft	322	97		
(There is no breakdown into two groups; limited to breast and axilla involved)				
J. Stewart Rodman <sup>7</sup>				
(Rodman operation)				
W. L. Rodman plastic closure	132	3		

The question of local recurrence (or persistence of carcinoma, as Hugh Auchincloss<sup>9</sup> has so aptly phrased it) is of interest from several angles. The surgeon is likely to consider a recurrence as a reflection on his lack of thoroughness and radicalism. It often may be so. But it must also be recognized that the most radical of surgeons cannot clean out the intercostal and intermammary nodes without removing the chest wall!

Then too, it is interesting to note the increase in the percentage of general and local recurrence the longer the cases have been followed. Like others, some of my patients have had local recurrences in the scar and adjacent skin at eleven, thirteen, and seventeen years after operation. But in only one

instance have I seen local recurrence alone. That patient had a local recurrence at eleven years, with excision, and freedom from disease, now seven years. The numerous other patients shortly revealed evidence of cancer elsewhere.

It is possible that cancer may lie dormant in subcutaneous or dermal tissue for many years and then flare up into renewed activity. Some day the biochemist may be able to give an answer to this clinical observation.

It is not my thought to weigh too carefully the variations in percentage except in a broad way. It may be pointed out that regardless of the Halsted or the Handley approach, there is a high incidence of local recurrence, and that there is no proof that one method is better than the other in avoiding local recurrence. It is also, I think, fair to believe that in cases with axillary metastases the local recurrence rate is tripled over those in which the cancer is limited to the breast.

It is a proper method to break down the cancer into two obvious groups: (1) limited to the breast, and (2) breast plus axillary metastases. At best this is a crude method for it must be recognized that cancer spreads by embolism to the lymph nodes along the intercostal and internal mammary spaces as well. It must always be borne in mind that the pathologic process is often more widespread than can be detected by either the clinician or the pathologist. It must also be admitted that there are limitations to the amount of surgery.

In our report of cases we have some support of our contention in the matter of local recurrence in patients with axillary metastases. It would seem to point to widespread emboli in the chest area. We have all along recognized that this index was crude, and acknowledged that at times we were innocently operating on patients who had already reached the stage of inoperability.

Recently, I have had an experience that threw some light on this subject.

#### CASE REPORT

Mrs. A. had a tumor in the right breast with axillary metastases.<sup>8</sup> At operation a biopsy was performed with a needle charged with a high-frequency current. The skin wound was then closed. Drapes were removed and the breast area was prepared again. Gowns, gloves, and instruments were changed, as if in preparation for another operation. The radical operation was then performed after the frozen section diagnosis of cancer had been made by the pathologist (Brandes). At the end of the operation, it became obvious that a skin graft would be necessary. The left thigh was prepared by an assistant, after which the operator, *without changing gloves*, took the Padgett-Hood dermatome and removed a suitable area of skin in one piece. Sulfathiazole ointment was applied to this raw skin by an assistant and the physician completed the operation. Three months later this patient developed adenocarcinoma on the donor site. In the operation no carcinoma tissue was seen as the incision had gone wide of the biopsy site. It is true that there were involved lymph nodes in the axilla which had been removed en bloc from the apex of the axilla downward and outward. It is fair to assume that some invisible cancer tracks had been cut through and that some of these cells adhered to the gloves, and were transplanted to the raw area on the thigh at the time that the graft was taken.

To draw an analogy from this case, it is fair to assume that in the course of a radical operation one must not infrequently cut through invisible cancer

tracks, and that some cancer cells deposit on the knife or gloves, to be deposited later about the raw wound. In an attempt to avoid this, we have made a practice of using arterial clamps only once, but we have not changed gloves frequently. We have used four or five scalpels in the course of an operation. It might be indicated to use many more. I believe now that one source of local recurrence is the unconscious deposit of cells about the wound.

It might be contended, with considerable truth, that in these cases we are operating in inoperable cases, even though we have no physical method of detection at the time of operation. Methods of technique for avoidance of cancer cells are as strongly indicated as avoidance of pus cells, but methods only are available. We can see neither. Theoretically, the endotherm needle might help to avoid this hazard, through cauterization and destruction of tissue. To date there has not been sufficient evidence to support this theory.

To return to the relationship of local recurrence to an initial widespread of the cancer at the time of the initial operation, I have observed that the local recurrence has been in association with the presence of metastases outside the operative field in every case in this series, except one. This exception was in a woman who had no axillary metastases at the initial operation. She was free from the disease for eleven years when she developed a local recurrence in the scar. This was excised and now, seven years later, she is well and free from signs of cancer.

We have also observed, with others, the development of cancer metastases in distant points such as the upper end of the femur, only to have local recurrence appear a year or two later. The longer a series of cases is followed, the higher will be the percentage of local recurrence.

Before the advent of roentgen therapy there was local recurrence. As the technique developed it was hoped by all of us that the thorough treatment of the operative field would reduce if not eliminate local recurrence. At least in that area roentgen therapy should prove itself. It has been our experience that such has not been the case. We have the same high incidence of local recurrence after the use of postoperative x-ray therapy.

#### SUMMARY

Local recurrence of breast cancer after radical mastectomy is a common experience in all clinics.

A chest without a skin graft is preferable to one with a skin graft. With the Handley technique it is usually possible to make a plastic skin closure.

As far as can be found out, there is no sufficient proof yet that the Halsted skin removal with Thiersch graft gives a reduced incidence of local recurrence over the plastic skin closure of Handley.

It is my belief that local recurrence after a proper radical operation such as the Halsted or Handley procedure is due to first, the physical impossibility of removing all cancerous tissue in the internal mammary and intercostal areas. In other words, we are dealing in such cases with undetectable, inoperable extension of the cancer; second, the transplantation of cancer cells that have

been cut into in the course of the operation. This frequency should be reduced by improved "cancer asepsis."

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# SURVIVAL RATES OF RADICAL MASTECTOMY FOR UNILATERAL AND BILATERAL CARCINOMA OF THE BREAST

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THE mammary gland is one of the most common sites of malignant disease in women. There are essentially two types of primary malignant neoplasm of the breast: carcinoma and sarcoma. Carcinoma is the principal type of malignant lesion occurring in the mammary gland. The different types of malignant lesions of the breast found in 6,558 patients on whom operation was performed at the Mayo Clinic from 1910 to 1940, inclusive, are shown in Table I.

TABLE I. MALIGNANT LESIONS OF THE BREAST (1910-1940 INCLUSIVE); RADICAL MASTECTOMY, TOTAL SERIES PATHOLOGIC DIAGNOSIS

TYPE OF LESION	NUMBER	PER CENT
Adenocarcinoma	6,412*	97.78
Epithelioma	31	0.47
Paget's disease	69	1.05
Melanoepithelioma	3	0.05
Sarcoma	39	0.59
Carcinosarcoma	4	0.06
Total	6,558	100.00

\*Includes 21 cases in which the pathologic diagnosis was made elsewhere.

The relative frequency of occurrence of the different types of carcinoma constituting 99.4 per cent of the total 6,558 malignant lesions of the breast in this series is very important from the standpoint of prognosis because this type of malignant neoplasm is prone to metastasize early to distant parts of the body, a fact that emphasizes the importance of early recognition and immediate treatment of malignant disease of the breast.

The results of treatment of malignant disease of the breast have been markedly improved by radical surgical treatment. Since the introduction of this method by Halsted, it has been the method most generally accepted by the medical profession.

This radical surgical treatment is based on the hypothesis that the malignant lesion is localized at the onset but that later in the course of the disease it invades other tissues by transmission through the lymph stream and occasionally through the blood stream. If this conception of the disease is correct, it is manifest that the most important considerations in the treatment are early recognition and immediate complete removal of the diseased tissues. One of the principal reasons for failure of surgical operation to accomplish this objective uniformly is the high percentage of cases in which metastasis has occurred before the patient is operated upon. If the condition is confined to the breast at the time of operation, complete eradication of the disease can be expected.

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From a surgical standpoint lesions of the breast may be divided into two general groups. The first group consists of those that can be definitely diagnosed clinically as malignant lesions. These are best treated by immediate primary radical mastectomy.

The second group consists of those lesions in which a definite diagnosis cannot be established on the basis of the clinical manifestations of the disease. This is the most important group from a surgical standpoint as the lesions are usually early and the most satisfactory operative results can be obtained from surgical treatment of these lesions. As I have stated before, in all cases in which there is a single localized tumor, the lesion should be completely removed by wide surgical excision and a definite diagnosis immediately established by microscopic examination from frozen sections of the tissue. If the lesion is found to be malignant, the operation should be completed immediately as a radical amputation.

From the standpoint of operative procedure the best surgical results are obtained from primary radical amputation. There are many variations in methods of carrying out the minor details of the radical amputation but the fundamental principles of the operation are invariable and should be carried out in all cases accepted for surgical treatment. This as an initial treatment is by far the most important procedure and the possibility of a cure depends on the thoroughness with which it is carried out. The importance of this cannot be overestimated, for secondary operative procedures are rarely curative. I believe that one of the important factors in the unsatisfactory results obtained from surgical treatment is the relative frequency with which minor operations are done for malignant disease.

The number of inoperable cancers of the breast that have been seen at the clinic during the last five years has remained fairly constant. There are varied opinions as to what constitutes operability. I shall state briefly the criteria of operability that have been followed in this series of cases. Any lesion of the breast was considered to be operable if it was freely movable from the thoracic wall regardless of ulceration. In some cases even if there were cutaneous nodules proximal to the tumor, regardless of the presence or absence of palpable axillary lymph nodes, the lesion was considered operable. In addition, patients were accepted for operation if they had a diffuse type of malignant growth, if malignant disease was associated with lactation, as well as if malignant disease was associated with pregnancy. Those conditions were considered to be inoperable in which a large growth was fixed to the thoracic wall and there was very extensive metastasis to the axillary and supraclavicular lymph nodes or metastasis to other distant parts of the body. A few patients who had metastasis that involved distant portions of the body were accepted for operation because of exceptional circumstances.

As thus indicated, it is difficult to draw any sharp line between operable and inoperable lesions and in each case treatment must be according to the findings. I have accepted for operation all patients to whom, I felt, there was a reasonable chance of offering comfort or greater length of life as well as



those whose disease, I felt, stood a reasonable chance of being cured. It may seem that these rules of operability have not been drawn strictly enough and that cases have been accepted for operation in which the growth is too extensive. This is a matter of opinion, however, and justification has been found in many cases in which the condition was thought to be absolutely hopeless before operation but in which the patients have lived to enjoy many years of comfort.

There are many factors that influence the results of surgical treatment, the more important of which are as follows: (1) the extent of the malignant involvement at the time of operation, (2) the thoroughness with which the radical operation is done, (3) the degree of malignancy as shown by microscopic examination of the primary lesion, (4) the presence of other associated conditions such as pregnancy, (5) the general constitutional diseases such as diabetes, (6) the age of the patient.

Statistical studies of the results of treatment of mass groups of patients are often misleading. This is particularly true when comparing the results obtained from different types of treatment; in these studies it is imperative that only similar groups of cases be used for comparison. I do not believe that comparative studies are of value unless it is definitely known that the groups compared are similar as to type and extent of the disease.

There are unavoidable inaccuracies in statistical studies because of the difficulty in obtaining accurate classifications of cases due to the many factors that influence prognosis as well as the difficulty in obtaining 100 per cent follow-up records of cases in which operation was performed, but these studies are the most valuable method we have of determining the results obtained from treatment. Their value is in direct proportion to the accuracy of classification, the completeness of the follow-up, and the length of time that has elapsed since treatment was instituted.

For the past nineteen years I have made statistical studies at about two-year intervals of the cases of carcinoma of the breast in which operation was performed at the Mayo Clinic. However, because of the influence of war conditions, an interval of four years has elapsed since the last study. There has been a slight decrease in the percentage of follow-ups from 98.5 to 97.1 per cent of traced patients. Even the latter percentage, however, I believe is a very high proportion because of the size of the series and present-day difficulties of contacting patients because of changes of residence.

The following statistical studies have been made on all patients on whom operation has been performed at the clinic for malignant disease of the breast from the years 1910 to 1940, inclusive, and comprise a series of 6,558 cases. Forty-seven patients (0.7 per cent) died in the hospital following operation; of the 6,511 patients who recovered from operation 6,318 (97.0 per cent) have been traced three or more years.

These studies have been made primarily to determine the results of radical surgical treatment as well as to point out some of the clinical or pathologic factors that influence the prognosis. In all of the statistical studies of survival

rates it has been assumed that the patient died of malignant disease although in many instances it was definitely known that death was due to other causes.

I should like to express my appreciation to the division of biometry and medical statistics for their diligence in searching for these records and in obtaining such a remarkably high percentage of traced patients.

The study of survival rates for the various periods after operation was made in the following manner. The records of patients on whom operation had been performed the requisite number of years prior to the time of inquiry, which was Jan. 1, 1944, were first selected. For the calculation of the three-year survival rate, the patients treated in 1940 or earlier were selected; for the five-year survival rate, those operated upon in 1938 or earlier were selected; for the ten-year survival rate, those operated on in 1933 or earlier were selected, and so forth. Obviously, then, the three-year survival rate was calculated on a larger number of patients than the five-year survival rate; the five-year rate was calculated on a larger number of patients than the ten-year survival rate and so forth. Of the patients operated upon, anyone not traced for a sufficient number of years after operation was considered untraced and was not included in the calculation of the survival rate. For instance, in calculating the five-year survival rate, a patient who had been operated on seven years prior to the time of inquiry but had been traced for only four years after operation, and who was living at that time, was considered untraced in the calculation of the five-year survival rate, because it is not known whether that patient did or did not survive until the fifth year after operation. For the purposes of the calculation of the three-year survival rate, that patient was considered traced, for it is known that the patient survived more than three years after operation.

When patients did not answer the routine follow-up letter, the local department of health, bureaus of vital statistics, and so forth were consulted to learn whether any record of death existed. In the end, only a small fraction of the patients remained untraced. Ninety-seven per cent of the patients on whom operation had been performed three or more years before investigation were traced for the requisite period.

The first study was made on the entire series of malignant lesions of the breast treated by radical mastectomy from 1910 to 1940, inclusive. All cases are included in this table, carcinoma, sarcoma, unilateral and bilateral disease, females and males. The special group studies which are shown later are included in this table. The objective of this study was to determine the influence that the extent of the disease, as indicated by the presence of axillary nodal metastasis, when found at the time of the operation, had on prognosis. The results of this study are shown in Table II, which gives for the three-year, five-year, ten-year, fifteen-year and twenty-year survivals, the number of patients on whom operation was performed, those traced, and the number who survived, with the respective percentages. This is the only table of survival rates in which the complete tabulation of these different numbers of patients will be included. In the subsequent tables that deal with survivals, only the

TABLE II. MALIGNANT LESIONS OF THE BREAST, RADICAL MASTECTOMY—MALES AND FEMALES, CARCI

	PA- TIENTS OPER- ATED ON*	PA- TIENTS TRACED	LIVED 3 OR MORE YEARS AFTER OPERATION		PA- TIENTS OPER- ATED ON	PA- TIENTS TRACED	LIVED 5 OR 10 YEARS AFTER OPERATION	
			PA- TIENTS	PER CENT OF TRACED PA- TIENTS			PA- TIENTS	PER CENT TRACED PA- TIENTS
AXILLARY METASTASIS								
Present (60%)	3,897	3,790	1,717	45.3	3,593	3,511	1,072	30
Absent (40%)	2,614	2,528	2,148	85.0	2,302	2,223	1,685	75
Total	6,511	6,318	3,865	61.2	5,895	5,734	2,757	48

\*Inquiry as of Jan. 1, 1914. The three-year group comprises the patients on whom operation was performed three or more years prior to the time of inquiry, that is, 1940 or earlier; the five-year group comprises those on whom operation was performed in 1938 or earlier; the ten-year group comprises those on whom operation was performed in 1933 or earlier and so forth. Ninety-seven per cent of patients were traced. The 47 patients who died in the hospital following operation (1910-1940) are included in the calculation of survival rates.

number of patients traced and the percentage of survivals will be given, in order to simplify the tables.

As is seen in Table II, there were, for the calculation of the three-year survival rate, 6,511 patients with malignant lesions of the breast on whom operation was performed in 1940 or earlier, of whom 6,318 (or 97.0 per cent) were traced. There was a wide variation in the survival results and the prognosis was much better in those cases in which axillary nodal metastasis was not found at the time of operation than it was in those cases in which axillary nodal metastasis was found. The patients who did not have axillary metastasis at the time of operation constituted 40 per cent of the entire series. The proportion of this group of patients living three years or more after operation was 85.0 per cent, or almost twice as large as that for the group with axillary metastasis, which was 45.3 per cent. In the five-, ten-, fifteen-, and twenty-year survival rates of patients without axillary nodal metastasis, it was found that the improvement increased progressively over the group with axillary metastasis. For the five-year period, the survival rate for the group without metastasis was two and one-half times as large as that for the group with metastasis; for the ten-year period it was three and one-half times as large; for the fifteen-year period it was four times as large, and for the twenty-year period it was more than five times as large.

Although axillary nodal metastasis is only one of the factors that may indicate the extent of the disease at the time of operation, I believe that it is one of the most important factors indicating the prognosis following operation because of the great influence that it has on the survival rates. Because of this fact, in compiling statistical studies of survival rates of malignant disease of the breast, I believe that all cases should be divided into two main groups, those with and those without axillary nodal metastasis at the time of operation, and that statistical studies should never be based on a combination of the groups, without knowing the number of patients in each group.

Accordingly, in all of the following studies of different classifications and types of carcinoma, the cases in each classification have been divided into two

SARCOMA, UNILATERAL AND BILATERAL DISEASE, SURVIVAL RATES ACCORDING TO AXILLARY METASTASIS

		LIVED 10 OR MORE YEARS AFTER OPERATION				LIVED 15 OR MORE YEARS AFTER OPERATION				LIVED 20 OR MORE YEARS AFTER OPERATION	
		PA-TIENTS TRACED	PER CENT OF TRACED PA-TIENTS	PA-TIENTS OPER-ATED ON	PA-TIENTS TRACED	PA-TIENTS TRACED	PER CENT OF TRACED PA-TIENTS	PA-TIENTS OPER-ATED ON	PA-TIENTS TRACED	PA-TIENTS	PER CENT OF TRACED PA-TIENTS
40	2,891	478	16.5	2,281	2,243	250	11.1	1,502	1,468	96	6.5
17	1,647	959	58.2	1,258	1,200	532	44.3	858	816	272	33.3
57	4,541	1,437	31.6	3,542	3,443	782	22.7	2,360	2,284	368	16.1

groups, those with and those without axillary nodal metastasis at the time of operation.

#### UNILATERAL CARCINOMA OF THE BREAST IN WOMEN

A study was made of all women patients who had unilateral carcinoma of the breast, to determine the results of radical mastectomy for this group of patients. The results of this study are shown in Table III. This study comprises a series of 6,149 patients or 93.8 per cent of the entire series of malignant lesions of the breast. Of these 6,149 patients, 5,970 (or 97.1 per cent) have been traced three or more years. Of the patients, 3,722 (or 60.5 per cent) were found to have axillary nodal metastasis at the time of operation and 2,427 patients (39.5 per cent) were not found to have axillary nodal metastasis at the time of operation. The three-year, five-year, ten-year, fifteen-year, and twenty-year results were very similar, varying only a fraction of a per cent from those in the entire series as shown in Table II. In those cases in which axillary metastasis was not present at the time of operation the results were much better than in those cases in which axillary nodal metastasis was present.

A study was made to determine if there was any difference in the results obtained in the different grades of carcinoma of the breast. I shall first give a brief summary of the grading of cases, which has been done according to Broders' method of dividing malignant lesions into four grades based on cellular differentiation. This part of the study is based on 5,134 cases, the total number that has been graded in the series of unilateral carcinoma in women. A study was also made to determine the percentage of cases in each of the four grades of malignancy and the percentage of each grade of malignancy with and without axillary nodal metastasis at the time of operation. The results of this study are shown in Table IV. It was found that 49.2 per cent, or nearly one-half of all carcinoma of the breast in this series, is of grade 4 malignancy and that of these grade 4 lesions axillary nodal metastasis was found in 84.1 per cent of cases at the time of the operation. On adding the grade 3 and 4 lesions, it was found that 81.7 per cent of carcinoma of the breast was of high grade malignancy from which metastasis occurred early. This again emphasizes the seriousness of malignant disease of the breast in

that the majority of the lesions are of a high grade of malignancy and present a high percentage of axillary nodal metastasis at the time of operation.

A study was then made to determine the survival rates according to the four grades of malignancy. The two main groups (those with and those without axillary nodal metastasis) were each subdivided into four groups, making eight classes in all. I believe that the comparison of results of any type of

TABLE III. UNILATERAL CARCINOMA OF THE BREAST IN WOMEN; SURVIVAL RATE FOR DIFFERENT PERIODS AFTER RADICAL MASTECTOMY; A COMPARISON OF RATES IN GROUPS WITH AND WITHOUT AXILLARY METASTASIS\*

AXILLARY METAS-TASIS	TOTAL	3 YEARS		5 YEARS		10 YEARS		15 YEARS		20 YEARS	
		PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS
Present (60.5%)	3,722	3,619	45.1	3,348	30.4	2,757	16.4	2,132	11.1	1,392	6.5
Absent (39.5%)	2,427	2,351	85.1	2,059	75.7	1,521	57.9	1,119	44.4	759	33.5
Total	6,149	5,970	60.9	5,407	47.6	4,278	31.1	3,251	22.5	2,151	16.0

\*Only patients operated on and traced for the different periods are included in this table.

TABLE IV. UNILATERAL CARCINOMA OF THE BREAST (1910-1940 INCLUSIVE); RADICAL MASTECTOMY, METASTASIS IN WOMEN BY GRADE OF MALIGNANCY

	TOTAL SERIES		WITH METASTASIS		WITHOUT METASTASIS	
	NUMBER	PER CENT OF TOTAL GRADED CASES	NUMBER	PER CENT OF RESPEC-TIVE GRADE	NUMBER	PER CENT OF RESPEC-TIVE GRADE
Grade 1	287	5.6	13	4.5	274	95.5
Grade 2	653	12.7	233	35.7	420	64.3
Grade 3	1,666	32.5	1,078	64.7	588	35.3
Grade 4	2,528	49.2	2,127	84.1	401	15.9
Total graded cases*	5,134	100.0	3,451	67.2	1,683	32.8

\*In 1,061 cases, grade of malignancy was not stated.

TABLE V. RADICAL MASTECTOMY FOR UNILATERAL CARCINOMA OF THE BREAST OF WOMEN; A COMPARISON OF SURVIVAL RATES ACCORDING TO GRADE OF MALIGNANCY WITH AND WITHOUT AXILLARY METASTASIS\*

AXILLARY METAS-TASIS	3 YEARS		5 YEARS		10 YEARS		15 YEARS		20 YEARS	
	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS	PA-TIENTS TRACED	PER CENT SUR-VIVALS
Present:										
Grade 1	13	92.3	12	100.0	11	63.6	10	40.0	8	25.0
Grade 2	228	70.6	209	53.1	185	34.6	160	24.4	131	14.5
Grade 3	1,039	55.1	933	35.3	777	17.6	620	10.6	423	5.2
Grade 4	2,048	37.1	1,903	24.9	1,495	12.5	1,063	8.2	687	5.1
Absent:										
Grade 1	261	96.9	203	95.1	108	88.0	58	74.1	36	55.6
Grade 2	407	91.6	348	84.2	231	65.8	120	44.2	47	25.5
Grade 3	563	82.8	468	70.5	287	50.9	159	37.1	81	28.4
Grade 4	383	75.7	309	62.8	193	43.0	132	30.3	81	21.0

\*Only patients operated on and traced for the different periods are included in this table. Total patients operated on: 6,149, of whom 5,970 were traced. Of those traced, in 1,028 the grade of malignancy was not stated.

treatment is most accurate when made according to this classification. Table V shows the results over periods of three, five, ten, fifteen, and twenty years according to the grade of malignancy and the presence or absence of axillary nodal metastasis at the time of operation. This shows a definite and uniform relationship between the operative results and the degree of malignancy, in that the lower the degree of malignancy the higher the percentage of patients alive three, five, ten, fifteen, and twenty years after operation. This was found to be true in both the groups with and without axillary metastasis.

It also shows, as was revealed in the previous studies, that the surgical results are much more satisfactory in cases without lymphatic involvement than in those with lymphatic involvement in the same grade of malignancy. The study shows that the grading of malignant lesions gives a very important indication as to the prognosis. I believe that the grading of malignant lesions represents one of the greatest advances that has been made in the study of malignant disease in recent years.

A study was made of all women patients who had had radical mastectomy for unilateral carcinoma of the breast between the years 1910 and 1940, inclusive, to determine the influence of age of the patient on the incidence of occurrence and results of operation. This constitutes a series of 6,195 patients, as is shown in Table VI. The youngest patient was 16 years and the oldest

TABLE VI. UNILATERAL CARCINOMA OF THE BREAST IN WOMEN; RADICAL MASTECTOMY (1910-1940 INCLUSIVE), AGE DISTRIBUTION AND INCIDENCE OF METASTASIS ACCORDING TO AGE

AGE (YEARS)	TOTAL PATIENTS	PER CENT	WITH METASTASIS	
			NUMBER	PER CENT
16-19	5	0.1	1	20.0
20-29	103	1.7	47	45.6
30-39	837	13.5	507	60.6
40-49	2,029	32.7	1,220	60.1
50-59	1,803	29.1	1,158	64.2
60-69	1,116	18.0	672	60.2
70-79	292	4.7	146	50.0
80-87	10	0.2	4	40.0
Total	6,195	100.0	3,755	60.6
Mean age 51.3 years				

was 87 years of age. In 32.7 per cent of the entire series the disease occurred in the fifth decade of life. This is the decade of life that presented the highest incidence of occurrence. The mean age of the entire series was 51.3 years. The highest incidence of metastasis found at the time of the operation in the different decades of life was 64.2 per cent and was found in patients from 50 to 59 years of age, inclusive. In 60.6 per cent of the entire series axillary nodal metastasis was found at the time of operation.

A study was made to determine the five-year survival rates according to age. This study was made on a series of 5,558 women patients, of whom 5,407 were traced. These patients had had radical mastectomy for unilateral carcinoma of the breast from 1910 to 1938, inclusive, which permits the compiling of five-year survival rates. The results of this study are shown in Table VII. This study shows that in patients having axillary nodal metastasis at the time

TABLE VII. UNILATERAL CARCINOMA OF THE BREAST IN WOMEN;  
FIVE-YEAR SURVIVAL RATES ACCORDING TO AGE

AGE (YEARS)	WITH METASTASIS			WITHOUT METASTASIS			TOTAL SERIES		
	PATIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION		PATIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION		PATIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION	
		NUM- BER	PER CENT		NUM- BER	PER CENT		NUM- BER	PER CENT
16-19	1	0	—	4	4	100.0	5	4	80.0
20-29	45	13	28.9	43	40	93.0	88	53	60.2
30-39	466	106	22.7	281	219	77.9	747	325	43.5
40-49	1,102	334	30.3	699	571	81.7	1,801	905	50.2
50-59	1,029	341	33.1	549	403	73.4	1,578	744	47.1
60-69	577	189	32.8	356	252	70.8	933	441	47.3
70-79	125	34	27.2	122	69	56.6	247	103	41.7
80-87	3	0	—	5	1	20.0	8	1	12.5
Total	3,348	1,017	30.4	2,059	1,559	75.7	5,407	2,576	47.6

of operation, the highest percentage of five-year survivals was in the sixth decade of life. In patients presenting no axillary nodal metastasis, the highest percentage of five-year survivals was in the second and third decades of life. However, in these decades of life there is a relatively small percentage of patients compared with the later decades of life. The best results in the later decades of life were obtained in the fifth decade, in which the proportion of five-year survivals was 81.7 per cent. This is also the decade of life that carries the greatest incidence of the disease.

A quinquennial study from the years 1910 to 1939 was made of some of the clinical and pathologic considerations to determine what change, if any, had taken place in these periods. This study is recorded in Table VIII and

TABLE VIII. UNILATERAL CARCINOMA OF THE BREAST IN WOMEN;  
RADICAL MASTECTOMY (1910-1940)

YEAR	TOTAL CASES	PER CENT WITH METAS- TASIS	PER CENT WITH GRADES 3 AND 4	MEAN AGE (YEARS)	PER CENT UNDER 50 YEARS	DURATION OF SYMPTOMS	
						PER CENT UNDER 6 MONTHS	PER CENT UNDER 1 YEAR
1910-1914	527	58.3	87.8	51.0	50.7	32.6	54.3
1915-1919	900	66.7	84.1	50.2	52.8	41.6	63.0
1920-1924	1,026	64.6	84.8	50.6	50.6	44.5	62.7
1925-1929	1,164	65.5	82.4	51.1	48.3	49.7	65.4
1930-1934	1,028	60.3	80.4	51.9	43.8	49.6	68.1
1935-1939	1,265	52.4	79.0	51.9	46.2	56.4	70.4
Total	5,910	61.2	82.0	51.2	48.3	47.5	65.1

shows very little change in the mean age of patients but it does show some tendency to an increase in age of patients at the time of operation in the past ten years. This is also reflected in the decreasing percentage of patients less than 50 years of age at the time of operation. It is gratifying to see that there was an appreciable decrease in the percentage of patients having axillary nodal metastasis in the past five-year period studied (1935-1939), it being 52.4 per cent as compared with 61.2 per cent of the total for the entire period, a fact that indicates that the educational program in which the medical pro-

fession has participated is showing favorable results in that physicians are seeing patients earlier in the course of the disease. This is also reflected in that there was a higher percentage of patients, 56.4 per cent, operated on within six months after the onset of symptoms during the last five-year period and 70.4 per cent within one year as compared with 47.5 and 65.1 per cent of the total periods in these respective groups. It is also found that there has been a tendency toward a lower percentage of grades 3 and 4 malignancies in the past fifteen years.

A quinquennial study was made of unilateral carcinoma of the breast in women who had had radical mastectomy from 1910 to 1938, inclusive. The last period is only four years (1935-1938) because patients operated on in 1939 had not been operated on for a sufficient length of time to enable five-year results to be compiled. This study was made up of 5,558 patients of whom 5,407 were traced. The patients are divided into the two groups, those with and those without axillary nodal metastasis at the time of operation, as is shown in Table IX. It was found that there was a consistent and appreciable

TABLE IX. UNILATERAL CARCINOMA OF BREAST, RADICAL MASTECTOMY; FIVE-YEAR SURVIVAL RATES FOR DIFFERENT PERIODS OF EXPERIENCE ACCORDING TO METASTASIS

PERIOD IN WHICH OPERATION WAS PERFORMED	WITH METASTASIS			WITHOUT METASTASIS			TOTAL SERIES		
	PA- TIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION		PA- TIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION		PA- TIENTS TRACED	LIVED 5 YEARS OR MORE AFTER OPERATION	
		NUM- BER	PER CENT		NUM- BER	PER CENT		NUM- BER	PER CENT
1910-1914	300	71	23.7	212	133	62.7	512	204	39.8
1915-1919	586	155	26.5	292	211	72.3	878	366	41.7
1920-1924	650	155	23.8	356	252	70.8	1,006	407	40.5
1925-1929	750	245	32.7	395	305	77.2	1,145	550	48.0
1930-1934	607	213	35.1	396	324	81.8	1,003	537	53.5
1935-1938 (4 years)	455	178	39.1	408	334	81.9	863	512	59.3
Total	3,348	1,017	30.4	2,059	1,559	75.7	5,407	2,576	47.6

improvement in the results obtained from radical mastectomy in each of the five-year periods. The study of patients presenting axillary nodal metastasis at the time of operation from 1910 to 1914, inclusive, shows that 23.7 per cent were living five years after operation as compared with 39.1 per cent of those on whom operation was performed during 1935 to 1938, inclusive. In this study the results obtained in patients without nodal metastasis at the time of operation show a greater improvement in that there was 62.7 per cent of five-year survivals from 1910 to 1914 as compared with 81.9 per cent from 1935 to 1938.

#### BILATERAL CARCINOMA

The results of the surgical treatment of bilateral carcinoma of the breast are shown for two classifications: (1) those in which the carcinoma occurred in the second breast at a later time, or nonsimultaneous carcinoma, and (2) those in which the carcinoma occurred in both breasts at the same time, designated as "simultaneous" carcinoma of the breast.



*Nonsimultaneous.*—The occurrence of nonsimultaneous carcinoma of the breast presents a very important problem in that some surgeons advocate the routine removal of the remaining breast in all patients on whom radical removal of one breast has been performed. I have made a special study of this group of patients in order to determine the incidence as well as the results of radical mastectomy for primary carcinoma of the remaining breast. The study of this group of cases has been divided into two main groups, in order to obtain as accurate an evaluation of results as possible. The first group consisted of patients who had both operations of radical mastectomy done at the Mayo Clinic. This consisted of a series of 155 patients. The intervals between the operations were from one to twenty-eight years.

The second group consisted of those patients who had either the first or the second operation done elsewhere. This comprised a series of fifty-seven patients. We have made a special effort in this latter group to determine definitely that the operation done elsewhere was for carcinoma and only those cases in which we had definite knowledge that the operation which was done elsewhere was for carcinoma have been compiled. In a previous paper, which I published in the *Pennsylvania Medical Journal*, January, 1940, this group of cases was larger. In the present study a number of these patients have been reclassified and have been retained in the group of unilateral carcinoma because of the lack of definite evidence that the operation done elsewhere was for carcinoma.

The entire group of nonsimultaneous carcinoma in this series is 212 cases and, when compared with unilateral carcinoma of 6,149 patients of this series, is 3.4 per cent. This, however, is the incidence of operable carcinoma occurring in the remaining breast in this series and not the actual incidence of carcinoma occurring in the remaining breast as there is probably an equal number of cases, if not a greater number, in which carcinoma of the remaining breast developed but which are inoperable because of distant metastasis from the first side. It has been impossible to determine accurately the percentage of this latter group of carcinoma occurring in the remaining breast but it is probable that the actual incidence is from 6 to 8 per cent. This percentage, while relatively high, does not warrant routine mastectomy of the remaining breast but it does indicate the importance of a routine follow-up examination on all patients on whom radical mastectomy has been performed for unilateral carcinoma of the breast.

The results of the study of the survival rates of women patients who had bilateral radical mastectomy for nonsimultaneous carcinoma of the breast in which both operations were done at the clinic are shown in Table X. There were 155 patients, all of whom were traced. The three-, five-, ten-, fifteen-, and twenty-year survival rates of this group were very satisfactory and when compared with results of unilateral carcinoma of the breast seem to be better, but it must be realized that this is a relatively small group of cases (155) and there was a much larger percentage of patients without axillary nodal metastasis. There was also a higher percentage of lower grades of malignancy. It must also be remembered that many of these patients live many years fol-

TABLE X. BILATERAL CARCINOMA OF THE BREAST IN WOMEN; BILATERAL RADICAL MASTECTOMY AT THE CLINIC FOR NONSIMULTANEOUS LESIONS; A COMPARISON OF RATES IN GROUPS WITH AND WITHOUT AXILLARY METASTASIS

AXILLARY METAS- TASIS	3 YEARS		5 YEARS		10 YEARS		15 YEARS		20 YEARS	
	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS
Present (48%)	75	64.0	73	43.8	61	32.8	56	25.0	35	14.3
Absent (52%)	80	90.0	74	85.1	58	63.8	36	44.4	27	37.0
Total	155	77.4	147	64.6	122	47.5	92	32.6	62	24.2

lowing the first operation before a carcinoma develops in the remaining breast, the longest interval being twenty-eight years. These survival rates are compiled from the date of the first operation. All of these factors influence the survival rates. It does indicate that even though carcinoma does develop in the remaining breast the results may be very satisfactory.

A study made of patients on whom bilateral radical mastectomy was performed for nonsimultaneous carcinoma of the breast in which either the first or second operation had been done elsewhere is shown in Table XI. This

TABLE XI. BILATERAL CARCINOMA OF THE BREAST IN WOMEN, BILATERAL RADICAL MASTECTOMY (FIRST OR SECOND OPERATION PERFORMED ELSEWHERE, FOR NONSIMULTANEOUS CARCINOMA) A COMPARISON OF RATES IN GROUPS WITH AND WITHOUT AXILLARY METASTASIS

AXILLARY METAS- TASIS	3 YEARS		5 YEARS		10 YEARS		15 YEARS		20 YEARS	
	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS	PA- TIENTS TRACED	PER CENT SUR- VIVALS
Present (55%)	31	48.4	30	30.0	25	8.0	18	0	13	0
Absent (45%)	25	68.0	24	62.5	19	52.6	10	10.0	8	0
Total	56	57.1	54	44.4	44	27.3	28	3.6	21	0

comprises a series of fifty-seven cases. The results shown in this study are not as satisfactory as those shown in Table X. It is impossible to determine definitely the cause for the marked difference of the survival rates in these two series because the extent as well as the grade of the disease of the side done elsewhere is not known but it is probably due to the fact that there was a higher percentage of patients in this group who had axillary nodal metastasis at the time of operation and the lesions may have been more extensive and of higher grade.

*Simultaneous.*—The results of the study of the three-, five-, ten-, fifteen-, and twenty-year survival rates of bilateral simultaneous carcinoma of the breast are shown in Table XII. This comprises sixty-two patients, or 1 per cent, of the entire series. This study shows that in forty-four, or 71 per cent, of patients nodal metastasis was found in either or both axillae at the time of the radical mastectomy. This percentage is higher than that found in the

TABLE XII. BILATERAL CARCINOMA OF THE BREAST IN WOMEN; BILATERAL RADICAL MASTECTOMY, SIMULTANEOUS OPERATIONS; A COMPARISON OF RATES IN GROUPS WITH AND WITHOUT AXILLARY METASTASIS

AXILLARY METAS- TASIS	PA- TIENTS	3 YEARS		5 YEARS		10 YEARS		15 YEARS		20 YEARS	
		PA- TIENTS TRACED	PER CENT SUR VIV- ALS	PA- TIENTS TRACED	PER CENT SUR VIV- ALS	PA- TIENTS TRACED	PER CENT SUR VIV- ALS	PA- TIENTS TRACED	PER CENT SUR VIV- ALS	PA- TIENTS TRACED	PER CENT SUR VIV- ALS
Present (71%)	44	42	28.6	39	17.9	30	3.3	24	0	18	0
Absent (29%)	18	15	66.7	13	61.5	6	50.0	5	40.0	3	0
Total	62	57	38.6	52	28.8	36	11.1	29	6.9	21	0

entire series, which was 60 per cent. No patients who had axillary metastasis survived to the fifteen-year period and only 3.3 per cent who had axillary metastasis survived the ten-year period. There were only eighteen cases in which no axillary nodal metastasis was found at the time of the operation. The results of this series were much more satisfactory than in the group in which metastasis was present but even in this group there was no patient who survived twenty years. These results show the seriousness of bilateral simultaneous malignant lesions, as they are much less satisfactory than the general results of the entire series and much less satisfactory than the results in cases of nonsimultaneous carcinoma of the breast.

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## Original Communications

### INTERRUPTION OF THE SYMPATHETIC NERVOUS SYSTEM IN RELATION TO TRAUMA

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TOTAL war has created a necessity heretofore unequalled of observing the effects of trauma applied to the human body in every conceivable form. As predicted by Livingston<sup>1</sup> and later pointed out by de Takats,<sup>2</sup> the opportunity, largely absent between wars, for studying any considerable number of cases of post-traumatic painful and vasospastic states has been revived.

Interruption of the sympathetic nervous system applies chiefly in three general categories, all of which are probably related to improvement of the circulation at the site of trauma. These groups are as follows:

(1) Post-traumatic painful and vasospastic states with or without Sudeck's osteoporosis. This group includes those cases where reconstructive surgery is contemplated in the presence of a dangerously reduced circulation.

(2) Injury of the main arterial supply of an extremity.

(3) Acute trauma, particularly fractures and crushing injuries of the hands and feet.

Out of the mass of material which is accumulating it is hoped that sufficient information may be obtained to clarify many of the perplexing problems which now confront the profession in dealing with these cases, thereby reducing discomfort, malfunction, and prolonged hospitalization in many individuals.

In this Army General Hospital in the Zone of the Interior, wounded have been received from all theaters of war and from surrounding station complements. It has been illuminating to observe the large number of individuals who have sustained mild or severe trauma of the extremities who are suffering, in addition, from vascular abnormalities and minor causalgia (Homans<sup>3</sup>) related to the trauma. These minor causalgias and vasospastic states complicating trauma result in considerable malfunction and delay in convalescence. When pain is severe, though not even reaching the degree of a true causalgia (Mitchell<sup>4</sup>), varying degrees of deterioration of the personality may, in time, result.

As examples of vasospastic and causalgic states complicating trauma, the following illustrative cases are cited.

#### CASE REPORTS

**CASE 1.**—A 28-year-old private had a past history indicating a rather unstable emotional make up, and his adjustment to Army life had not been very satisfactory. In September, 1944, this soldier experienced a sudden sharp pain in the right middle finger. There was no previous injury or known inciting cause. A diagnosis of tenosynovitis was made and a lateral incision on one side of the finger was carried out. It is stated that a drop or two of pus was obtained, but the history is not too clear on this point. The incision healed quickly leaving a nonadherent scar. Concomitant with this episode the hand became cold and sweated profusely. Its color varied from bright pink in a warm environment to livid on exposure to cool air. Pain was a predominant feature, and prohibited any use of the hand. Physical therapy increased the pain. Pressure on any part of the hand was borne with difficulty and there was a continual dull ache which seemed to be situated deep in the palm and occasionally shot to the elbow. The patient's sleep was interfered with and he became increasingly nervous and apprehensive. He was admitted to this hospital Nov. 9, 1944, at which time it was noted, in addition to the findings mentioned, that the tissues of the right hand were swollen, the normal creases were shallow or obliterated, and the skin was atrophic and shiny. The color changes were striking, as previously noted (Fig. 1). The patient stated that all the fingers felt stiff. Limitation of flexion of the fingers was present. X rays of the right hand (Fig. 4) showed a moth eaten osteoporosis (Sudeck's). The patient's appearance suggested the possibility of hyperthyroidism, but investigation along this line produced negative results.

Nov. 13, 1944, a novocain block of the right stellate ganglion was done. The hand became warm and pink and remained so for four hours. During this time the pain was decreased, but returned with all its previous intensity. The improvement with blocking definitely implicated the sympathetic nervous system. Since the amelioration of symptoms was of short duration, and in view of the patient's mental state, a permanent interruption of the appropriate sympathetic fibers was decided upon in preference to a continuation of novocain blocks. Sympathectomy was done on Nov. 20, 1944. The hand became warm and dry and there was a change in the consistency of the soft tissues in twenty four hours. Edema disappeared, the normal creases became deeper, and motion of the fingers was less restricted (Fig. 3). There was a steady diminution of pain so that in about two weeks normal pressure of the hand caused no discomfort and the subjective discomfort was much improved. There was no further radiation of the pain to the elbow. X ray of the hand about four weeks post operatively (Fig. 4) showed an almost normal bony structure. Unfortunately, the patient's psychoneurotic manifestations showed only slight improvement and he was discharged on a Certificate of Disability.

**CASE 2.**—A 22-year old private mangled his left thumb in a wood router three years before admission to this hospital on Nov. 21, 1944. The injury resulted in extensive scarring of the soft tissues of the thumb with deformity and limitation of motion of this digit. The hand became cold and moist and presented the color changes described in Case 1, although more severe (Figs. 5 and 6). Pain was an outstanding feature in this case. The hand was kept continually in the pocket to keep it warm and away from trauma. The slightest touch on the thumb was unendurable and because of this, use of the hand was prohibited. None of the modalities of physical therapy could be tolerated. On several occasions, novocain blocks of the thumb had been done to permit trimming of the nail. X rays showed typical Sudeck's osteoporosis. Infiltration of the tight scar on the thumb with 2 per cent novocain enabled the thumb to be moved without pain, but deep pressure was still painful and there was no release of vasospasm of the hand. Three successful novocain blocks of the left stellate ganglion produced the characteristic changes in the hand and cessation of pain, but the effects lasted only about one half hour. Undoubtedly a sympathectomy should be performed on this patient, following which the desirability of plastic and orthopedic procedures

Fig. 1.



Fig. 2.



Fig. 3.

Fig. 1.—Appearance of hands two weeks prior to operation, showing edema of dorsum, right hand, and fingers; the shiny atrophic condition of skin of fingers is apparent.

Fig. 2.—The mottled cyanotic appearance of the right hand is well shown.

Fig. 3.—Condition of right hand one week after right dorsal sympathectomy; the skin is wrinkled and less shiny, and there is no color difference in the two hands.

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on the thumb can be evaluated. His surgical program is still under consideration. It is noteworthy that this patient does not show marked personality changes except for a rather natural tendency to remain withdrawn from others and to play a spectator's role both at work and recreation.

CASE 3.—A private was admitted to this hospital on Sept. 28, 1943. July 26, 1943, he had sustained compound comminuted fractures of the left tibia and fibula and paralysis of the common peroneal nerve. There were also extensive soft tissue lacerations and bruising in the left calf. At the time of the injury preliminary débridement was carried out. The leg was placed in a plaster cast. The patient was extremely ill and numerous transfusions were given. There were several changes of plaster. After final removal of the cast, physiotherapy was commenced, consisting of massage, whirlpool baths, and baking. X-rays of the ankle showed typical spotty osteoporosis of the tarsal and metatarsal bones. The ankle was swollen and tender to palpation.

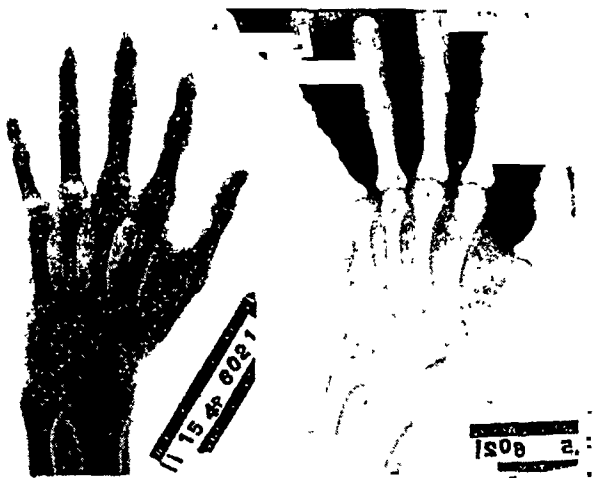


Fig. 4.—Comparative x-rays of the right hand. A, Showing osteoporosis, was taken one week prior to sympathectomy. B, showing almost normal calcification, was made four weeks after sympathectomy.

As time went on the patient continued to be unable to tolerate weight-bearing due to pain. It was noted that the foot was cold, moist, and blue, though arterial pulsations were present. There was limitation of motion of the ankle and foot in addition to the effect of the peroneal paralysis. One lumbar sympathetic block was done with an excellent response in the foot. In view of the long program ahead of this patient, including eventual dissection of the peroneal nerve, a left lumbar sympathectomy was done on Feb. 14, 1944. The response to operation was most gratifying and achieved more than had been hoped for. Subjective improvement in ankle comfort was marked. In about two weeks partial weight-bearing was commenced. Calcium deposition was noted in the bones of the foot. The patient was transferred to a neurosurgery center.

CASE 4.—Aug. 4, 1944, near St. Lo, a 33-year-old private first class received a gunshot wound of the left foot, with fractures of the os calcis, cuboid, navicula, and shafts of the second, third, and fourth metatarsi. After initial débridement and application of a cast he was evacuated to England, where pulp traction was applied to the second, third, and fourth toes. Traction was maintained for six weeks. On Sept. 1, 1944, a new cast was applied. At this time the wounds were entirely healed. He was admitted to this hospital Nov. 9, 1944, wearing a cast. The patient was given a weight-bearing cast, but the ankle continued to be painful. X-rays (Fig. 7) showed a persistence of marked osteoporosis of the distal tibia, tarsi, and metatarsi. On Feb. 22, 1945, the cast was removed and active physiotherapy started, consisting of paraffin and whirlpool baths. The patient was encouraged to walk up to three





Fig 7.—Extreme osteoporosis is shown eight months after the original injury, the upper picture shows some of the old fractures

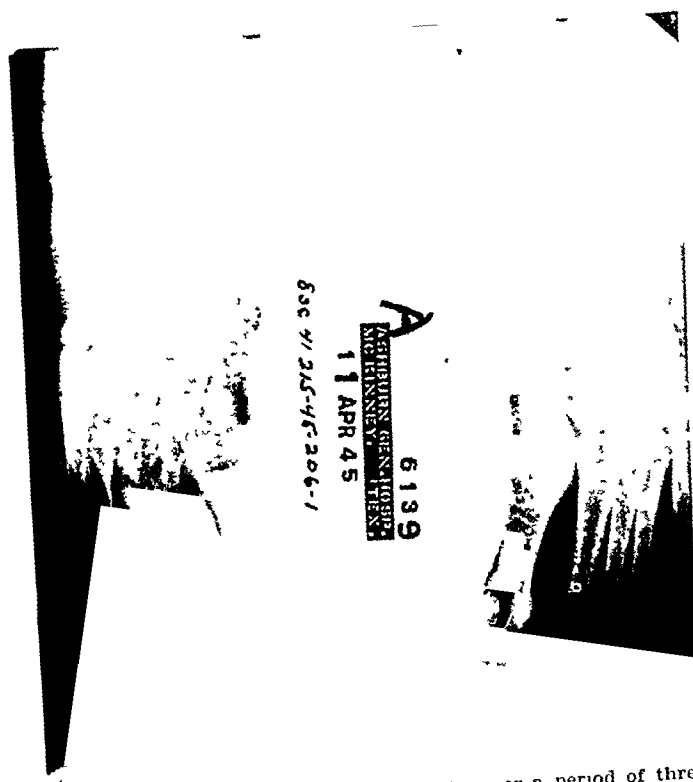


Fig 8—X-ray views taken after five lumbar blocks over a period of three weeks showing diminution of osteoporosis patient's foot is now comfortable and he is ambulatory without support

Fig. 5.



Fig. 6.



Fig. 9.



Fig 10

Fig 5—The scar and deformity of the thumb are shown, with marked discoloration of the thumb and dorsum, the thumb nail has been allowed to grow because of pain caused by trimming it

Fig 6—Comparison of both hands shows the shiny atrophic condition of the skin of the left hand, together with color changes

Fig 9—The scarring of the right palm and discoloration of right hand are shown

Fig 10—The dorsum of the right hand and fingers is swollen, there is an ulcer of the nail bed on the fourth finger.



miles per day, but pain was still present and there was swelling of the ankle. No improvement in the osteoporosis was noted. The foot was cold, blue, and usually moist. Occasionally it became warmer than its mate, although at such times it had a dusky hue. March 22, 1945, a series of novocain blocks was instituted. After the first block the patient was subjectively improved and could walk much better. The foot remained warm and dry for about twenty-four hours. After five blocks the appearance of the soft tissues and the patient's ability to walk were sufficiently improved to justify a period of observation. X-rays taken at this time, three weeks after the first block, showed greatly diminished osteoporosis (Fig. 8).

CASE 5.—A private first class, 30 years of age, was admitted to the hospital in August, 1944. His transfer diagnosis was trench foot and, on questioning, it was learned that this soldier had been fighting for a period of thirty days in the cold mountainous area of Italy without removing his shoes and stockings. The immediate course was typical of trench foot with marked swelling of the feet, bleb formation, and pain. The residual symptoms consisted of the usual pain on weight-bearing, but he had marked tingling and showed irrefutable evidence of vasospasm of both feet. A novocain block on the right side on Sept. 15, 1944, caused the foot to become warm, pink, and dry for several hours and the patient was subjectively relieved for the same length of time. Nov. 13, 1944, a right lumbar sympathectomy was done. The response in the right foot was satisfactory and the patient was almost immediately relieved of the discomfort. He was insistent upon having the other side operated upon.

This, of course, is not the constant picture in the late stages of trench foot. The degree of vasospasm varies and not all cases are suitable for sympathectomy. Each case must be individualized, a period of physiotherapy tried, and test blocks of the sympathetic nervous system carried out. Two of our patients have had sympathectomies with complete relief of symptoms in each instance. One patient has returned to full duty and the other will probably do likewise.

When reconstructive surgery is indicated in the later repair of the effects of trauma, an adequate circulation is an essential in insuring good healing and function. Adequacy of the vascular bed is a prime requisite in all plastic procedures and it is probable that one should hesitate to perform an arthrodesis, bone graft, or other major procedure in an area where Sudeck's osteoporosis is marked and the soft tissues demonstrate the presence of severe vasospasm. It is a relatively simple matter to determine the effect of a temporary block before the reparative procedure is undertaken. Decision as to whether a series of novocain blocks before and after surgery or a permanent sympathectomy should be done will depend upon the adequacy of the response to one or two test blocks and upon the length of the reconstructive program which the patient is to undergo. In some instances it may be considered that the reconstructive surgery itself will release the vasospasm, as, for example, in amputation of a digit or release of scar tissue involving a peripheral nerve trunk. However, when a long plastic or orthopedic program is planned, particularly if prolonged immobilization of the extremity is necessary, sympathectomy is preferable to innumerable novocain blocks.

CASE 6.—A private first class, aged 25 years, cut his right hand in a crosscut saw in June, 1944, and sustained compound fractures of the phalanges of the third, fourth, and fifth fingers and laceration of the flexor tendons of all digits except the thumb. This resulted in extensive scar contracture of the palm of the right hand with limitation of flexion and extension of the fingers. On admission to this hospital in October, 1944, the hand was



extensor tendons and a sensory branch of the radial nerve. There were chip fractures of some of the metacarpi. There was a deep, firm cicatrix across the wrist with almost complete loss of motion at the wrist joint and complete loss of extension of the fingers. In addition, it was observed on admission at this hospital that the dorsum of the hand was edematous. The skin of the entire hand was blue, moist, and cold. The patient's discomfort was increased on exposure to cold.

Proper splinting and various modalities of physical therapy were carried out over a period of weeks in an effort to increase wrist motion and improve the circulation. There was no real improvement. It was obvious that extensive plastic repair of the wrist scar was indicated and that the extensor tendons would have to be repaired. The plastic procedure was advisable as the first step so that good tissues would be present for further reconstructive surgery on the tendons. Doubt was entertained as to the adequacy of the circulation in the recipient area to permit proper healing of the proposed pedicle flap. A dorsal sympathectomy was done in June, 1944, with an excellent effect on the circulation in the hand. The edema

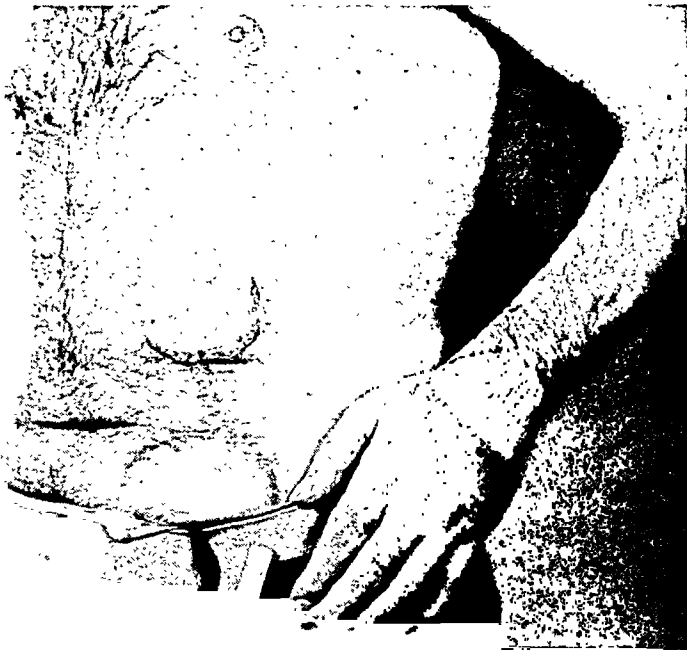


Fig. 12.—Plastic surgery carried out after left dorsal sympathectomy; excellent healing resulted.

disappeared. Subjectively the patient's hand felt much better. During the following weeks function improved at the wrist. A pedicle from the abdomen was transferred to the wrist by Major Kerwin Mareks and excellent healing resulted (Fig. 12). The patient was transferred to a hand center for further reconstructive surgery. A letter from this patient states that he now has almost complete use of the fingers.

Sympathetic block or sympathectomy when the main arterial supply of an extremity has been interrupted has saved many limbs. Due to the conditions which often are present at such time, it is usually better to institute novocain blocks immediately and await stabilization of the patient's condition before contemplating sympathectomy. The latter procedure may not even be necessary to prevent gangrene if blocks are carried out early and often.

CASE 8.—In June, 1944, a sergeant, 29 years of age, sustained a shell fragment wound of the left femoral artery 5 cm. above the level of the knee joint. The artery and vein were ligated and a series of lumbar sympathetic blocks was immediately instituted and continued over a period of days. For five days amputation seemed imminent, but collateral circulation developed and no actual gangrene occurred. On admission to this hospital in September, 1944, the patient had a rather marked limp and complained of weakness and numbness in the left leg and foot. There were no striking color changes in the left foot but it was cooler than the right and there was considerable atrophy of the calf. There was definite weakness of the calf muscles. After a thirty-day furlough there was no change in the patient's condition. Meecholy iontophoresis was given three times a week without benefit. In September, a left lumbar sympathetic block produced a striking improvement of the circulation in the foot. In October, a left lumbar sympathectomy was done. There was an immediate improvement in the patient's subjective sensations in the leg. Strength returned rapidly in the next few weeks and the patient was returned to full duty.




Fig. 13.—The mummified condition of the left foot is shown. There are ischemic ulcers at the tips of the first and third toes.

CASE 9.—In February, 1944, a private received a perforating wound of both thighs and right knee from artillery fragments. The left popliteal artery was severed. Emergency surgery was carried out almost immediately with ligation of the left popliteal artery. No sympathetic blocks were performed. Two days later a left lumbar sympathectomy was done. Dry gangrene developed, involving the tips of the first, second, and third toes and all of the fourth and fifth toes. The fourth and fifth toes were amputated in June in the United States. On admission of the patient to this hospital the left foot looked almost mummified. There was atrophy of the skin and subcutaneous tissue and the forefoot and toes were stiff (Fig. 13). There were chronic ischemic ulcers of the first and third toes. The foot, however, was warm and dry. After a period of treatment with paraffin and galvanic baths there was practically no improvement, and the patient was transferred to an amputation center for evaluation. Maximum vasodilatation had been achieved in this case by the sympathectomy.

The inclination is to believe that the two-day interval between the injury and the sympathectomy may explain the gangrene, since it is likely that in this time there was enough

damage to the soft tissues of the foot from ischemia so that arteriolar dilatation, when achieved, was too late. Of course, it is possible that without sympathectomy in this case more tissue would have been lost than will now be the case.

Some interest has recently been aroused in the possibilities of subjecting acute injuries of the extremities to early sympathetic interruption, usually by novocain block, the rationale in this treatment being the immediate improvement in the circulation with resultant reduction of edema and an earlier return of the soft tissues to a normal state. The delayed effects of such therapy have yet to be evaluated, but it is entirely possible that the disability from crushing injuries about the wrists and ankles may be reduced due to an early lessening of edema and prevention or lessening of osteoporosis. The boggy, cold, and painful ankle which follows a Pott's fracture is well known. Disability of twelve to fourteen weeks or longer is anticipated with this fracture, due not so much to failure of bony union as to soft tissue changes with mild or severe vasospasm and osteoporosis of varying degrees, with pain and swelling on weight-bearing.

Work along this line was carried out in a neighboring station hospital where many acute injuries were seen. The results of this investigation will undoubtedly be reported in the near future. From our own small series of acute injuries treated in this manner, two representative cases are presented here for illustration.

CASE 1.—A private, 26 years of age, was admitted to the hospital on April 1, 1945, having sustained a fracture of the right ankle eight hours previously. He had walked about one-half mile after the accident and at the time of entry there was brawny edema of the foot and ankle and pronounced ecchymosis. X-rays revealed a fracture of the tip of the external malleolus and two fractures of the tibial malleolus. A satisfactory block of the left lumbar ganglia was obtained and as soon as vasodilatation occurred the patient found that he could voluntarily move his ankle in all directions without pain. Painless reduction of the fracture was obtained without further anesthesia and a nonpadded cast was applied. On the following morning, thirty-six hours after the injury, there was wrinkling of the toes, indicating a lessening of edema. Three subsequent daily lumbar blocks were performed. One week after the injury the cast seemed somewhat loose and it was, therefore, removed. The ecchymosis was still severe, but in other areas the edema of the foot and ankle was greatly reduced.

CASE 2.—A sergeant from the reconditioning section sustained a severe sprain of the right ankle on April 5, 1945. There was swelling and ecchymosis about the external malleolus and the patient was unable to bear his full weight on this side. A lumbar sympathetic block was performed and there was immediate reduction of pain. He was able to walk without help. An elastic bandage was applied and the patient told to remain in quarters. Two hours later, however, he engaged in a game of baseball and played five innings.

For full evaluation of the results of this treatment in such cases, a prolonged follow-up of numerous cases is necessary. It is conceivable, especially in the fracture cases, that, in addition to the immediate improvement in discomfort and swelling, some of the late effects may be avoided. There might be a lessening of osteoporosis and vasospasm in the later course which would result in an earlier resumption of function.

#### SUMMARY AND DISCUSSION

Novocain block of the sympathetic outflow and permanent sympathectomy have been discussed in relation to three main categories of post-traumatic conditions, comprising:



(1) Post-traumatic painful and vasospastic states with or without Sudeck's painful osteoporosis. In this group are included those patients needing reconstructive surgery in an area where the circulation is dangerously decreased.

(2) Injuries of the main arterial supply of an extremity.

(3) Acute injuries, particularly fractures and crushing injuries of the hands and feet.

Illustrative cases in all three groups are described where some form of sympathetic interruption was carried out. It is pointed out that a large percentage of patients who have sustained injuries of the extremities have prolonged pain and disability, often associated with vasospasm and osteoporosis, and that in these individuals permanent or repeated temporary interruption of the sympathetic outflow often results in a reduction in discomfort, malfunction, and prolonged hospitalization. Where extensive plastic or orthopedic procedures are contemplated, vasospasm and severe osteoporosis should be corrected prior to reconstructive surgery. Though application of these principles *early* in the presence of acute injuries of the hands and feet has not been given extensive trial, there is reason to believe that a reduction of both the early and late results of trauma to the soft tissue and bone may be achieved by sympathetic paralysis.

In view of the large proportion of individuals who show vasospastic changes after trauma of the extremities, it behooves the medical profession to be on the alert to discover and treat these manifestations.

After prolonged immobilization of an extremity in plaster there is usually a diminution of the blood supply, resulting in a cold hand or foot. The extremity may also show varying degrees of cyanosis. If this condition does not improve promptly in three or four days of active physical therapy, one novocain block of the appropriate sympathetic fibers may suffice to relieve the condition. If, however, the condition returns and vasospasm is clearly present, particularly if accompanied by osteoporosis, a series of blocks should be given, making one or two injections per week. If sufficient permanent improvement does not result after five or six blocks, and if there is the usual pain and swelling on weight-bearing, much valuable time will be saved if a permanent sympathectomy is performed. This is done only if the test blocks have been shown to give temporary relief.

Probably a reduction of disability could be achieved if vasospasm and osteoporosis were looked for during the period of immobilization and blocks carried out where indicated.

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# ABDOMINAL APOPLEXY SECONDARY TO RUPTURED "CONGENITAL" ANEURYSM

## MULTIPLE ANEURYSMS OF THE INFERIOR PANCREATODUODENAL ARTERY WITH RUPTURE OF ONE

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THE spontaneous rupture of a medium-sized intra-abdominal blood vessel independent of trauma, malignant tumor, or ectopic gestation has been termed "abdominal apoplexy." Although the rupture of an arteriosclerotic vessel is the usual cause of this rare condition, Bruce<sup>1</sup> in 1937 suggested that the rupture of a small "congenital" aneurysm might be responsible in some cases, particularly in the earlier age groups. Schuster<sup>2</sup> (1937) shortly thereafter described multiple aneurysms of the splenic artery which she believed were of congenital or developmental origin in a case of familial hemorrhagic telangiectasia. Nevin and Williams<sup>3</sup> (1937) described a case of massive spontaneous intraperitoneal hemorrhage due to rupture of a "congenital" splenic aneurysm associated with multiple aneurysms of the branches of the circle of Willis. It is the purpose of this paper to report another case, which by its instructive histologic picture adds further support to the concept of aneurysm secondary to congenital defect in the arterial wall, and to discuss the recent literature on this subject.

### CASE REPORT

J. O., a white man, aged 50 years, was admitted to the ward surgical service of the Jefferson Medical College Hospital on Dec. 25, 1943, with the chief complaint of epigastric pain.

For the past several years the patient had occasionally experienced a burning sensation in the epigastrium about two hours after eating, relieved by the taking of alkali. At 8 P.M. on Dec. 24, 1943, he experienced sudden, moderately severe, continuous, epigastric pain radiating straight through to the back, associated with slight nausea. The pain persisted throughout the night, preventing sleep. The following morning he drank a glass of milk which was promptly vomited. Because the pain failed to subside he made his way to the hospital at noon and upon arriving grew faint and collapsed, but did not lose consciousness.

Systemic review, past medical history, and family history contributed nothing of significance.

*Physical Examination.*—The patient appeared apprehensive, pale, and slightly cyanotic. The skin was cold and clammy. Temperature was 97° F.; pulse, 120; respirations, 26; blood pressure, 70/40. The pupils were of equal size and reacted to light and accommodation. The heart and lungs were essentially normal. On abdominal examination there was no limitation of diaphragmatic excursions. There was moderate tenderness, but no rebound tenderness, in the epigastrium and slight upper rectus muscle guarding. Peristalsis was normal. Rectal examination was negative. The extremities were normal.

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The clinical diagnostic impressions on admission were penetrating peptic ulcer or acute pancreatitis.

*Laboratory Studies.*—Hemoglobin was 84 per cent; red blood cells, 4,100,000; white blood cells, 13,400; color index, 1.02. Urinalysis was normal. Wassermann and Kahn serologic studies were negative. The blood urea nitrogen was 14.0 mg.; sugar, 73 mg.; serum proteins, 5.2 Gm.; and serum amylase, normal. A plain roentgenogram of the abdomen was normal.

*Further Progress.*—Following the intravenous administration of concentrated plasma and fluids, the patient's condition improved and the blood pressure rose to 120/90. Wangersteen suction was instituted. The pain diminished, at no time requiring medication for relief, and the abdominal tenderness and muscle guarding gradually subsided. Because of the marked improvement, conservative therapy was continued. The following day the temperature was normal; pulse, 100; hemoglobin, 71 per cent; red blood cells, 3,500,000; and white cell count, 9,000. At this time 500 c.c. of whole blood were administered. The patient continued to improve, was pain free, and except for a fluctuation of temperature between normal and 101° F. appeared to be in excellent condition.

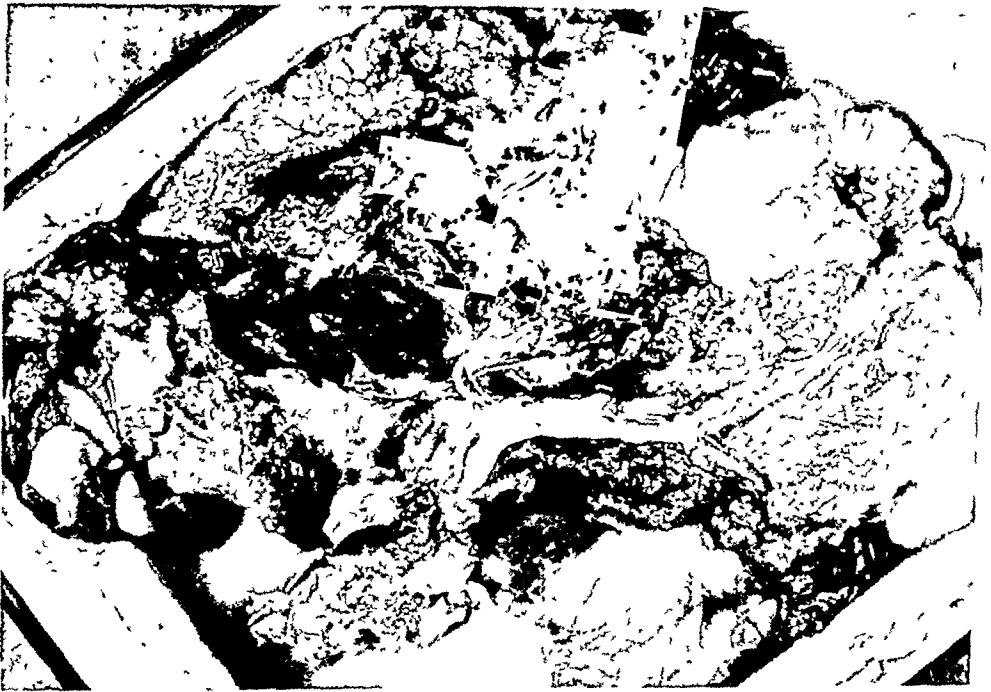


FIG 1—Gross specimen, showing the superior mesenteric and inferior pancreaticoduodenal arteries. Arrows point to the ruptured saccular aneurysm at the first bifurcation. Note the extravasated blood in the vicinity of the vessels.

At 9 P.M. on Dec. 29, 1943, the patient again complained of epigastric pain accompanied by a feeling as if something had broken, and went into the same shocklike state as on admission. Blood count at this time revealed a hemoglobin of 71 per cent; red blood cells, 3,000,000; and white cells, 12,000. The sedimentation rate was 36 mm. within forty five minutes. The pulse was 120, blood pressure, 94/60, and the abdominal findings as on admission. He again improved following the administration of plasma and fluids intravenously. It was thought at this time that the patient might have a dissecting aneurysm of the abdominal aorta. At 6 A.M. on Dec. 30, 1943, he again went into shock and died.

*Post-mortem Examination.*—

*Gross:* The peritoneal cavity contained approximately 1,200 c.c. of fluid and clotted blood. In addition, there was extensive hemorrhage into the retroperitoneal tissue of the

upper abdomen, particularly into the pancreas, transverse mesocolon, and around the upper portion of the aorta and right kidney. The head of the pancreas contained the greatest amount of hemorrhage and was partially destroyed by it.

The inferior pancreaticoduodenal artery, arising from the superior mesenteric, pursued a normal course for 3 cm. until its first bifurcation. At this point there was a sacculated aneurysm about 4 cm. in diameter, the ostium of which measured 1 cm. in length and 3 mm. across (Fig. 1). It was filled with a gray, laminated, antemortem clot and was in direct communication with the hemorrhagic material distributed throughout the pancreas and elsewhere. In the peripheral portion of the same artery there were three fusiform dilatations, not in relation with bifurcation angles. The lumens of two of these were ragged and contained antemortem blood clot. The remainder of the mesenteric artery, the celiac axis with its branches, and the portal vein were normal.

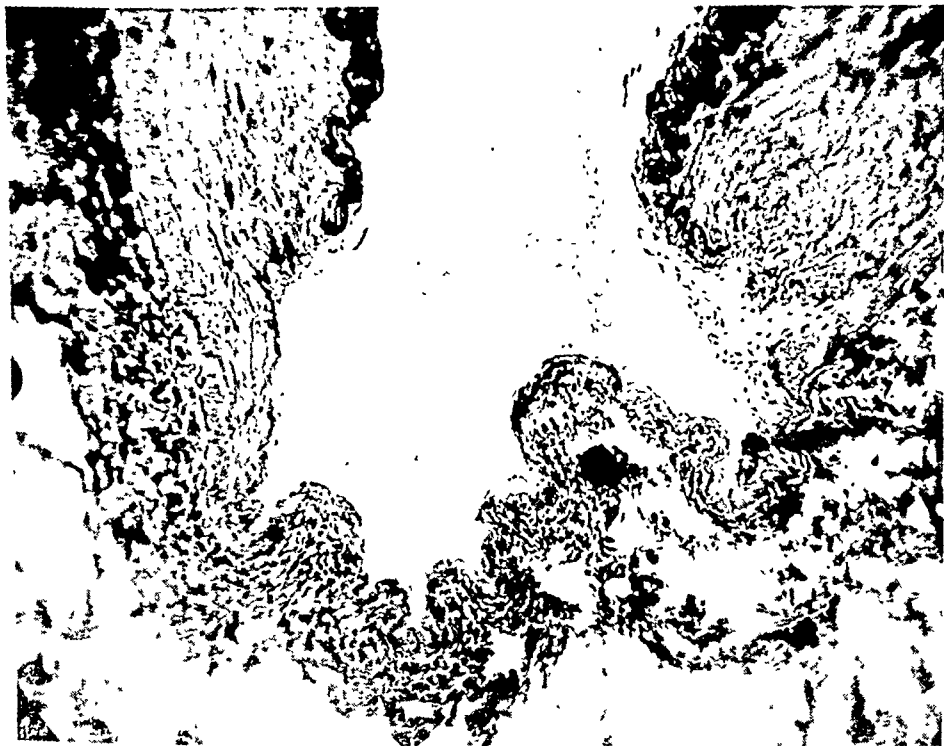


Fig. 2.—Inferior pancreaticoduodenal artery distal to the ruptured saccular aneurysm, showing a defect in the intima, internal elastic lamina, and all but the outer portion of the media. Note the partial covering of the inner portion of the media to the right by the internal elastic lamina, the presence of a few elastic fibrils in the floor of the defect, and the absence of inflammation in the adventitia and surrounding tissue. Elastic tissue stain with van Gieson counterstain ( $\times 100$ ).

The aorta and pulmonary vessels contained a smooth glistening intimal surface throughout. The heart was essentially normal and the coronary arteries showed moderate arteriosclerosis but no occlusions. The basilar vessels of the brain did not show any atherosclerosis or small aneurysms.

*Histologic Examination:* The entire inferior pancreaticoduodenal artery was blocked and several sections taken from each block. They were stained with hematoxylin and eosin and with Weigert's elastic tissue stain, using picric acid and acid fuchsin as counter stain. In the following description they are considered in the order in which it is thought the lesions evolved.

Sections of the main portion of the vessel just beyond the large aneurysm disclosed a small defect in the intima, internal elastic membrane, and all but a small rim of the outer

portion of the media (Fig. 2). One side of the defect showed a gradual attenuation from within out, while the other was more abrupt. The inner half of the media of the latter was covered with both the intima and the internal elastic membrane. The outer half of the media on this side was covered with a few edematous fibroblasts. Only a fraction of the inner portion of the media on the opposite side of the defect was covered with the internal elastic membrane. The rest was bare. The floor and base of the defect consisted of a very thin strip of the outer portion of the media in which there were a few elastic fibers. The adventitia and surrounding connective tissue were normal, showing no inflammation or hemorrhage. In the outer quarter of the media on each side of the defect there was some erythrocytic extravasation. Elsewhere the media and the remaining coats of the vessel were normal.

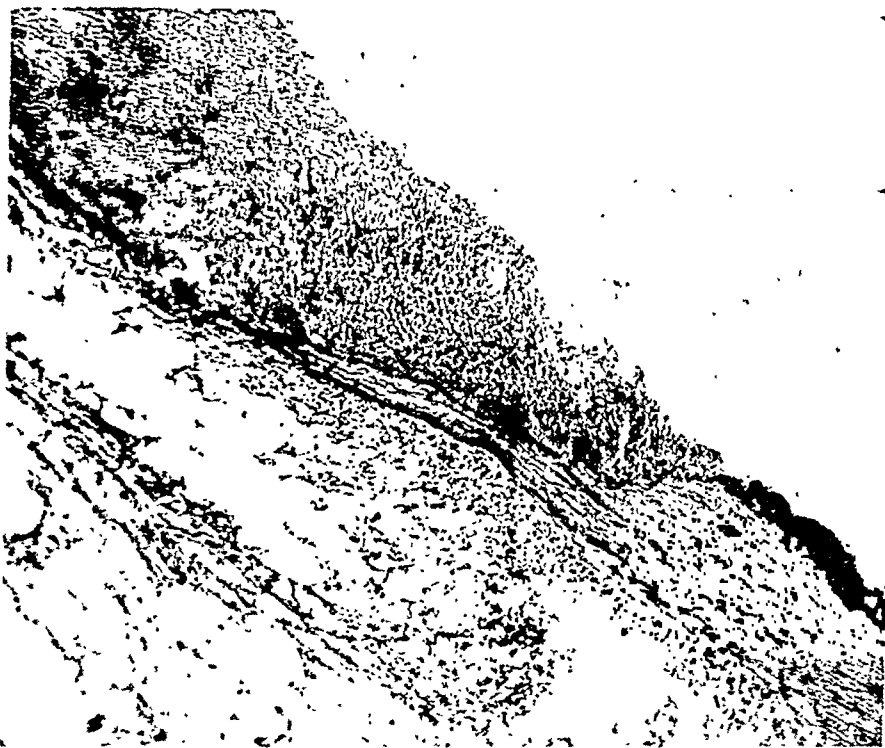


Fig. 3.—Section of one of the distal aneurysmal dilatations, showing a sudden termination of the intima and internal elastic lamina and a gradual attenuation to complete disappearance of the media. The floor of the defect is filled with recently coagulated blood. Elastic tissue stain with van Gieson counterstain ( $\times 50$ ).

In another area there were two similar but more superficial and saucerlike defects in the vessel separated from each other by a small island of relatively normal wall. These defects differed from the former in that (1) the walls showed a more gradual slope, (2) the outer third of the media was still intact and formed the floor, and (3) the adventitia and surrounding connective tissue were replaced with recent granulation tissue composed of fibroblasts, capillaries, and varied numbers of plasma cells, lymphocytes, and polymorphonuclear leucocytes. Further out there was extensive extravasation of erythrocytes.

The walls of the distal aneurysmal dilatations were similar to those previously described with the exception that in each the edges of the defects were widely separated; all the media had disappeared and the concavity was filled with varying amounts of recently coagulated blood (Fig. 3).

The wall of the aneurysm at the first bifurcation disclosed a sloping defect in its coats similar to those already described. This gradually disappeared in a mass of extravasated

blood. Sections of the wall of the peripheral portion of this aneurysm disclosed no remnants of a vessel. They were composed of extensive erythrocytic extravasation throughout the fat and connective tissue with only occasional islands of granulation tissue. Sections of other vessels in the vicinity of this pancreaticoduodenal artery and of the inferior pancreaticoduodenal artery in twelve consecutive autopsies disclosed no pathologic changes.

#### DISCUSSION

Although grossly the only changes seen in the artery were a ruptured sacular aneurysm at the first bifurcation and three small fusiform dilatations in the more distal portions of the vessel, the microscopic sections disclosed a defect along its entire course. The many sections furthermore showed various degrees of involvement and so permitted the following reconstruction of the probable train of events. Originally there was a congenital or developmental defect along the entire course of the artery consisting of what appeared to be a complete or partial failure of fusion of the media. At first this defect was most likely covered on its inner surface with the internal elastic membrane and the intima, but as the vessel was stretched these coats were broken, leaving a portion of the media and the adventitia or in some areas the adventitia alone to form the entire remaining wall. That the internal elastic membrane and the intima did at one time cover the defect is given some support by finding the former still covering a portion of the defect in some of the sections (Fig. 2). Where the dilatation of the artery was minimal, as in the distal three aneurysms, the defects were filled with recently coagulated blood. Where the dilatation was so great as to cause a complete break in the adventitia, as in the aneurysm at the first bifurcation, there was massive hemorrhage not only into the immediately adjacent tissue and along the vessel but throughout the retroperitoneal space. The onset of the hemorrhage was apparently coincident with the first attack of pain about five and one-half days before death. Proof of this is seen in the recent periarterial granulation tissue observed in most of the sections.

Aneurysms of branches of the abdominal aorta, regardless of type, are rare. From the literature and their own experience, Malloy and Jason<sup>4</sup> (1942) collected eighty-five cases of hepatic artery aneurysm; Machemer and Fuge<sup>5</sup> (1939), eighty-four cases of the splenic; and Lowsley and Cannon<sup>6</sup> (1943), seventy-five cases involving the renal artery. Single and multiple aneurysms unassociated with inflammatory or degenerative change have been reported, but only in the cases of Schuster<sup>2</sup> and Nevin and Williams<sup>3</sup> was a medial defect at the bifurcation angle described. On the other hand, intracranial aneurysms, most frequently the so-called "congenital" type, are found in 0.8 per cent of all post-mortem examinations according to Fearnside<sup>7</sup> and in 1.5 per cent according to Schmidt.<sup>8</sup>

The concept that single or multiple aneurysms might in some instances be due to a congenital defect in the arterial wall was first introduced by Eppinger<sup>9</sup> in 1887. This concept was investigated by Forbus<sup>10</sup> (1930), who demonstrated the association of miliary aneurysms of the superficial cerebral vessels with a characteristic defect in the tunica media at the angle of bifurcation of the arteries. This muscularis defect was shown to date from embryonic life. During development, the main trunk of the vessel receives its muscular coat at an

earlier period than the branches. The corresponding coat of the branch is then formed not as a direct extension from the parent trunk, but separately as a condensation from the surrounding mesenchyme. Fusion of the coats at the angle of origin of the branch may be faulty and thus result in an area of congenital focal weakness in the vessel wall. Forbus did not conclude that the aneurysm in its fully developed state is a congenital malformation *per se*, but an acquired lesion arising from a combination of focal weakness in the arterial wall on the basis of a congenital muscular defect, and degeneration of the internal elastic membrane as the result of continued overstretching of this membrane.

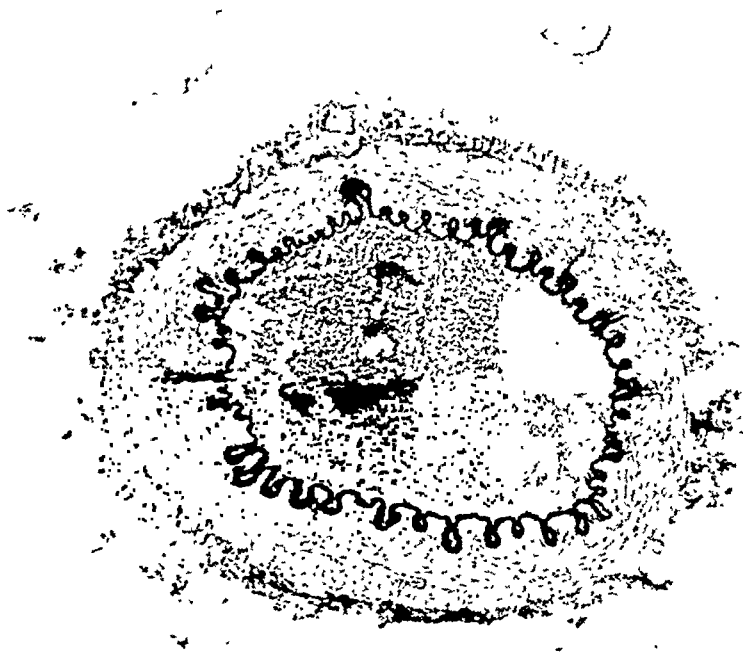


Fig. 4.—Section of a cerebral artery, showing the elastic tissue almost entirely concentrated in the internal elastic lamina. Elastic tissue stain with van Gieson counterstain ( $\times 50$ ).

Developmental defects of the media at the angles of arterial bifurcation are relatively frequent in cerebral, coronary, pulmonic, abdominal, and other medium-sized vessels, but the incidence of associated aneurysms is greatest by far in the cerebral ones. Glynn<sup>11</sup> (1940) stated that in thirty-seven out of forty-seven nonaneurysmal cases (approximately 80 per cent) there was a defect in the media at the angle of bifurcation of cerebral vessels, and he therefore questioned the etiologic relationship between these defects and aneurysms. He attempted to demonstrate by means of simple inflation experiments with vessels bearing natural or artificial medial defects that the internal elastic lamella is of greater relative importance in maintaining the form of the cerebral arteries. He concluded that the greater frequency of these aneurysms in the circle of Willis must be due to a difference in the topography of the elastic tissue of these vessels. According to this author as well as others (Hackel,<sup>12</sup>

Cobb and Blain<sup>13</sup>), in cerebral vessels almost the whole of the elastic tissue is concentrated in the internal elastic lamina (Fig. 4), and by reason of this position is probably more susceptible to injury and degeneration than if it were more widely distributed through the media and adventitia as in other vessels (Fig. 5).

Richardson and Hyland<sup>14</sup> (1941) in an exhaustive study of intracranial aneurysms stated that the medial defects are probably developmental and play a role in the formation of aneurysms, but that there is in addition an unrecognized acquired lesion causing degeneration of elastic tissue. They conclude that at present complete knowledge as to the cause of these aneurysms, frequently referred to as "miliary," "berry," "bifurcation," "congenital," or "developmental," is lacking.



Fig. 5.—Section of a mesenteric artery, showing the elastic tissue concentrated in the internal and external elastic lamina, and also dispersed throughout the media. Elastic tissue stain with van Gieson counterstain ( $\times 50$ ).

The case of Nevin and Williams<sup>3</sup> represents the first in the literature in which massive intraperitoneal hemorrhage is reported secondary to rupture of an aneurysm of an intra-abdominal vessel associated with a defect in the medial coat at the bifurcation angle. The present report represents a second case in which the aneurysm may be designated as "congenital" or developmental because of its multiplicity, location at the bifurcation angle of a medium-sized artery, small size, and association with a defect of the muscularis.

The case of Budde,<sup>15</sup> in which bleeding occurred from a side branch of the left gastroepiploic artery, must be excluded from the group under dis-



cussion since no definite aneurysm was visualized, a section of the vessel was not removed, and the cause was undetermined. The only reference we could find to aneurysms of the inferior pancreaticoduodenal artery was that of Bortolozzi<sup>16</sup> who described an unruptured fusiform arteriosclerotic aneurysm of this vessel discovered post mortem in a patient who died of carcinoma of the head of the pancreas.

The clinical features of abdominal apoplexy have recently been reviewed by Berk, Rothschild, and Doane.<sup>17</sup> Their analysis of twenty cases revealed nothing pathognomonic in either the symptoms or signs that would permit the diagnosis with certainty. The usual findings consist of abdominal pain, signs of peritoneal irritation, and the general manifestations of internal hemorrhage. All these features were present in our case, but the lesion was not diagnosed, since the possibility of its existence was not considered. Ligation of the bleeding point was employed in 80 per cent of this series, with recovery in 69 per cent. The prognosis is excellent if a definite bleeding point can be found, since in no case was there a recurrence reported following operation.

#### SUMMARY

1. A case of abdominal apoplexy secondary to rupture of one of multiple "congenital" aneurysms of the inferior pancreaticoduodenal artery is reported.
2. A "congenital" aneurysm is characterized by its frequent multiplicity, small size, location at the bifurcation angle of a medium-sized artery, and association with a defect in the muscularis.
3. The clinical features consist of abdominal pain, signs of peritoneal irritation, and the general manifestations of internal hemorrhage.

#### CONCLUSIONS

1. Massive intraperitoneal hemorrhage resulting from the rupture of "congenital" aneurysms of branches of the abdominal aorta is exceedingly rare in comparison to the analogous condition in cerebral arteries.
2. The rupture of a "congenital" aneurysm should be suspected when abdominal apoplexy occurs in patients without marked arteriosclerosis or hypertension.
3. Early operation, with excision of the aneurysm, would seem to offer the best chance of recovery.

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*Penicillin Levels in Blood, Pleural, and Spinal Fluids.*—Blood levels determined from time to time upon patients receiving penicillin at three-hour intervals by intramuscular injection and by constant intravenous and subcutaneous drip were comparable to those reported by others.<sup>1, 10, 11</sup>

The instillation of 40,000 units of penicillin intrapleurally in cases of empyema yielded levels of 2.5 to 9.9 Oxford units per cubic centimeter in the pleural fluid twenty-four hours later and therapeutic amounts of the agent persisted for five days after the initial instillation. Intramuscular injections of

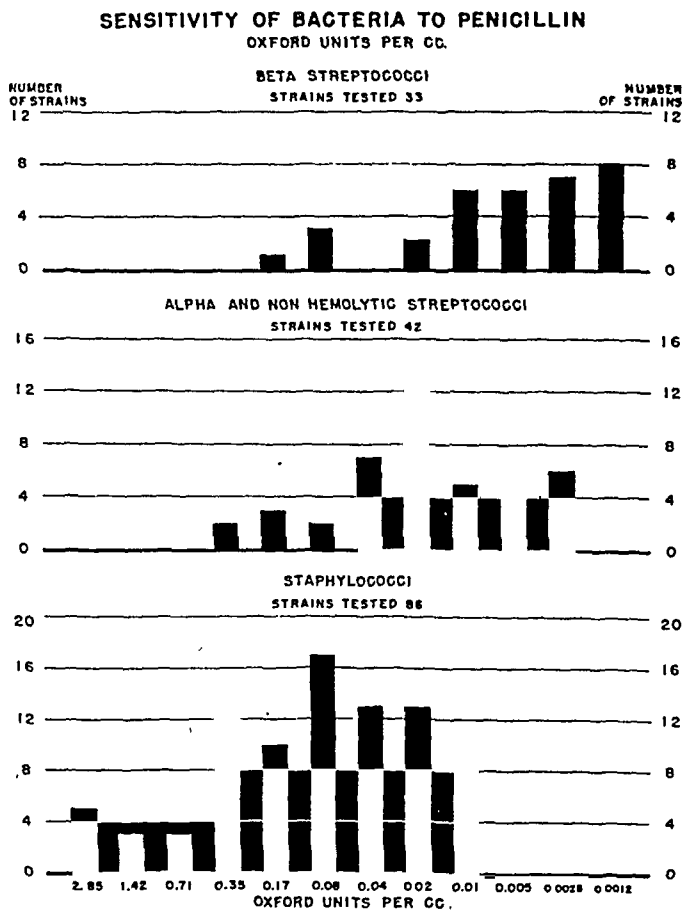


Fig. 1.—Sensitivity to penicillin of streptococci and staphylococci from present series.

60,000 units of penicillin at three-hour intervals produced levels of .156 to .312 units per cubic centimeter in a tuberculous pleural effusion. However, in the pus of established empyemas, intramuscular dosages of 25,000 units every three hours achieved insignificant penicillin concentrations (0 to .078 Oxford units).

Spinal fluid assays in ten patients undergoing parenteral therapy up to 480,000 units a day for other than central nervous system infections revealed the merest traces of penicillin. On the other hand, intrathecal injections of 10,000 to 20,000 units were followed by fluid levels of from 5.0 to 19.0 units

per cubic centimeter twelve hours later and by levels of 0 to 2.45 units (average 0.69) twenty-four hours later. The lumbar route of injection is the simplest and is usually adequate. The drug in two cases was observed to pass freely from the spinal into the interventricular fluid. In an earlier case,<sup>12</sup> however, this passage failed to occur. Also, we have clinical reasons to believe that in some cases cisternal injections are more effective than the lumbar.<sup>13</sup>

In one early peritonitis, fluid assay revealed .039 units one hour after 40,000 units penicillin were injected intramuscularly.

#### ANALYSIS OF CLINICAL MATERIAL

The analysis of clinical material covers 255 conditions in 220 patients for which penicillin treatment was administered. The cases to follow have been classified as disease entities and surgical or medical problems rather than according to the organisms cultured.

##### *Soft Tissue Infections.—*

*Carbuncles and furuncles* (13 cases): The morbidity of carbuncles and furuncles has been markedly reduced from that to be expected with sulfonamide therapy. The number of days until the lesion was nearly healed averaged 9.25 days for the carbuncles and 10 days for the furuncles. That external application of penicillin is of no benefit in these infections is well illustrated by the case of a young aviator treated for furunculosis of the scalp by local applications of penicillin in tragacanth jelly (250 units per cubic centimeter). The lesions soon reached such alarming proportions that intramuscular injections of 15,000 units every three hours were started. Within forty-eight hours the furuncles had melted down to tiny crusted papules.

In a number of instances it was observed that the carbuncle or furuncle, especially when the patient was given a heavy initial dose of penicillin, within twenty-four to thirty-six hours became more angry, swollen, and painful, the patient often feeling more toxic than before. There would then, within the next few hours, follow swift regression of the lesion, usually with suppuration and relief of pain. We have interpreted this Herxheimer-like reaction as possibly a clinical indication of a definite lysis of the staphylococcus and liberation of its endotoxin.

In no instance was it necessary to incise and drain a penicillin treated carbuncle or furuncle. Rapid liquefaction and spontaneous drainage invariably occurred. Our only interference was to pluck out the necrotic slough which formed with unusual rapidity.

*Cellulitis and abscess of soft tissue in general:* In a group of twenty cases our clinical appraisal in comparison with what might have been expected with sulfonamide drugs was as follows:

Result equal to sulfonamides	5
Result superior to sulfonamides	10
Exceptionally good result	4
Failure	1

Five times in this series penicillin overcame an infection after sulfonamides proved ineffectual. The one failure in the group was in a case of peculiar multiple burrowing sinuses of the arms and legs which baffled all diagnosis and treatment.

Cases 1, 2, and 3 from this group were of particular interest.

CASE 1.—Chronic ulcers of the toes in a patient with thromboangitis obliterans, that had for months resisted all other treatments, healed in two weeks under penicillin.

CASE 2.—A very severe cellulitis with abscess formation of the left cheek (see Fig. 2) which had grown progressively worse on adequate sulfadiazine therapy rapidly resolved under local treatment, consisting of aspirating the pus (containing alpha streptococci and *Staphylococcus albus*) and injecting locally, through the same needle, 25,000 units of penicillin on six occasions.



Fig. 2.—Patient (Case 2) with severe cellulitis of face, not of salivary or osteomyelitic origin; temperature ranging from 101 to 102° F. A, At start of local penicillin therapy, B, on fourth day of local penicillin therapy.

CASE 3.—A patient with diffuse subcutaneous abscesses of several fingers harbored highly penicillin susceptible staphylococci. In spite of penicillin dosages increased to 40,000 units intramuscularly every three hours, no response was obtained until multiple incisions were performed releasing pus under tension. Once drainage was established, the infection quickly subsided. This illustrates the impotence of penicillin against infection involving pus in closed spaces, however small.

*Infected operative wounds:* Seven cases of infected operative wounds include three inguinal herniorrhaphy wounds, a bilateral radical upper neck dissection, a laparotomy wound, a large secondarily closed wound of the hip, and

a primarily closed pilonidal sinus wound. With the exception of the pilonidal excision wound, all healed solidly and essentially per primam within an eighteen-day average, after one or two skin stitches had been removed to allow escape of pus. Staphylococci were isolated from four of these and hemolytic streptococci from the other two.

The pilonidal wound infected with staphylococci and a highly resistant fecal streptococcus proceeded to complete breakdown while receiving 120,000 units of penicillin a day.

*Threatened and established cavernous sinus thrombosis:* Six cases are summarized in Table I. It will be observed that four cases, although not full blown,

TABLE I. PENICILLIN IN THREATENED AND ESTABLISHED CAVERNOUS SINUS THROMBOSIS

CASE NO.	AGE	DIAGNOSIS	BACTERIOLOGY	PENICILLIN	RESULTS
1	24	Threatened cavernous sinus thrombosis, left, following nasal operation	Beta hem. Str. coagulase positive; hem. Staph. aureus	380,000 U. in 3 days	Worse after 48 hr. on sulfa; rapid subsidence under penicillin
2	26	Threatened cavernous sinus thrombosis from furuncle, left nostril	Blood stream and wound; hem. Staph. aureus	4,960,000 U. in 22 days	Worse after 36 hr. on sulfa; pulmonary infarcts, subsided without residuals
3	26	Threatened cavernous sinus thrombosis from frontal sinusitis	Hem. Staph. aureus; Beta hem. Str.	1,965,000 U. in 10 days	Orbital cellulitis subsided by 4th day and frontal sinusitis by 9th day
4	20	Threatened cavernous sinus thrombosis from ethmoiditis	Ethmoid sinus; Pneumococcus type 10	2,225,000 U. in 9 days	Orbital cellulitis subsided by 4th day and apparently was cured by 10th day
5	20	Cavernous sinus thrombosis, left; fungus infection of skin	Blood culture; negative nostril; hem. Staph. aureus coagulase positive	4,890,000 U. in 16 days	Sinus thrombosis cured but died from uncontrollable fungus skin ulcerations
6	19	Cavernous sinus thrombosis and multiple brain abscesses	Hem. Staph. aureus; anaerobic Str.	615,000 U. in 1 day	Moribund <sup>†</sup> with sepsis both of brain and of sinus; died

were called "threatened cavernous sinus thrombosis" by the ophthalmologic consultants because of early papilledema, ophthalmoplegia, or both, along with the marked orbital cellulitis and conjunctival edema. One patient (Case 2), shown in Fig. 3, had a positive staphylococcus blood culture and several pulmonary infarcts. Patients (Cases 5 and 6) with established cavernous sinus thrombosis died. One (Case 6) also had multiple brain abscesses and was moribund on entry. Another (Case 5) at the outset received 90,000 units of penicillin by intravenous drip. His condition growing rapidly worse, the dose was increased to 360,000 units daily and heparin and dicoumarin were given. Thereafter the major infection regressed satisfactorily. Then, after surviving the cavernous sinus thrombosis, he developed multiple rapidly necrotizing ulcerations of the face, groin, and thighs to which he finally succumbed. Repeated cultures, aerobic, anaerobic, and for fungi, revealed only *Staph. albus* and a fungus "rarely pathogenic to man," *Gomphaneria Petrosi*.

*Penicillin as Adjunct to Surgical Procedures.—*

*In extensive clean or in contaminated operative cases:* The sixteen cases include the following.

Nine patients with radical block dissections of the neck received 160,000 to 200,000 units daily with average total of 1,700,000 units. One hundred twenty thousand units daily would probably have sufficed. All healed per primam; none developed more than slight amount of fluid beneath the skin flaps; one developed marked facial edema and two moderate edema; one developed temporary minimal wound infection. A nontreated neck dissection during this period developed a severe streptococcal wound infection.



Fig 3.—Patient (Case 2, Table I) with threatened cavernous sinus thrombosis, staphylococcemia, and multiple pulmonary infarcts, secondary to furuncle, left nostril. A, Day following commencement of penicillin; B, sixth day after commencement of penicillin

One patient having developed marked facial edema following bilateral upper block dissection of the neck and another with postoperative hematoma and drainage following excision of a branchial cleft cyst, both subsided nicely without infection on the drug.

The wounds in a baby with a harelip operation and an adult who underwent a difficult excision of a recurrent thyroglossal fistula both healed per primam.

Three patients with extensive shell fragment wounds received prophylactic penicillin: one with an avulsion wound of the buttock and one with laceration of the liver healed without infection. The third with a large tear in the rectum communicating with a shattered upper femur developed a blood stream



infection with hemolytic streptococcus, *Str. fecalis*, and *Staph. albus* and died in spite of one-half million units of penicillin a day. We have so far received from overseas no survivors of a rectal injury communicating with a compound fracture of the femur.

*Excision and closure of granulating wounds:* Of granulating wounds there were twenty-four wounds in sixteen soldiers with an over-all success in seventeen and failure in seven. These wounds almost universally cultured *Staph. aureus* and *Staph. albus*, a few also contained *Str. faecalis*, *diphtheroids*, and *B. coli*. From Table II it can be seen that the largest number of failures occurred among

TABLE II. PENICILLIN IN EXCISION AND CLOSURE OF GRANULATING WOUNDS

DESCRIPTION	PENICILLIN DOSAGE	RESULTS
Ten decubiti in 3 paraplegias	200,000 U. daily	5 successful, 5 failed
One decubitus in a paraplegia	Local instillation through fine tube	Successful
Four amputation stumps	120,000 to 240,000 U. daily	3 drained thin staphylococcus-containing fluid but healed soundly; 1 failed
One reamputation 2 inches above infected amputation through knee	200,000 U. daily	Healed soundly after draining staphylococcal fluid
Eight granulating abscesses or infected sinuses	120,000 to 240,000 U. daily	7 healed per primam though one drained a scant amount; 1 failure in a small sinus of thigh

the decubiti, that the closed amputation stumps usually healed after a period of seropurulent drainage culturing staphylococci, and that wounds and sinuses (Figs. 4 and 5) almost always healed nicely.

It should also be mentioned that during the present study a decubitus receiving no other treatment than local boric compresses was excised and closed with per primam healing.

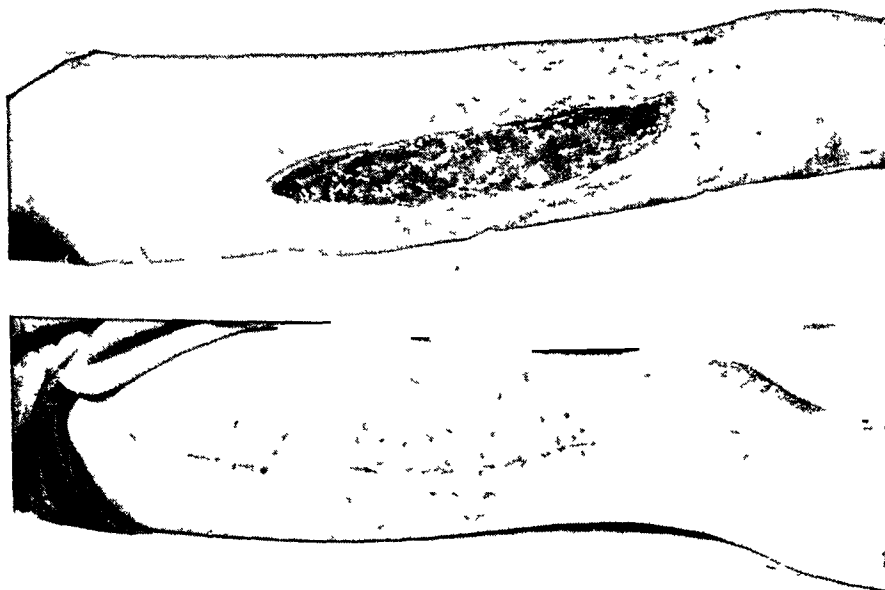
From the patient shown in Fig. 4 with a laminectomy wound, hemolytic *Staph. aureus*, sensitive to 2.85 Oxford units, was cultured; yet the wound cleaned up remarkably well allowing secondary closure twenty-nine days after the original laminectomy and while still harboring staphylococci. The granulating wound of the patient shown in Fig. 5 still cultured staphylococci at time of closure, yet per primam healing ensued. Such cases demonstrate a powerful factor supplied by the host which, in conjunction with penicillin, achieves clinical results unsuspected from cultures and in vitro sensitivity tests.

*Pilonidal sinus excision and primary closure:* Under a daily intramuscular dosage of 200,000 units of penicillin, eleven recently infected pilonidal sinuses in ten patients were excised and primarily closed using fine silk or cotton technique. Six broke down and five healed per primam. Staphylococci were present in all the failures and in two of the successful closures. This is a poor percentage for penicillin compared to the good results obtained in excision and closure of soft tissue wounds elsewhere with similar flora. It would seem to attest to the local peculiarity of anatomy of the lesion as well as to the local bacteriology. It was our clinical impression that local penicillin with or without the parenteral administration somewhat facilitated healing by granulation even when primary closure had proved unsuccessful.



Fig 4—Epidural abscess necessitating surgical excision of laminae, fifth to eleventh dorsal vertebrae inclusive, secondarily closed twenty-nine days postlaminectomy. Photograph taken three days after secondary closure, healed by first intention.

A.



B

Fig 5—Subfascial abscess of right thigh of life-endangering severity, complicating operation on knee joint and not responding to sulfonamide therapy. A, Twenty-two days following radical incision and drainage, and nineteen days after start of penicillin. B, eighteen days after secondary wound closure, done twenty-four days after incision and drainage.

*Skin grafting:* It is interesting that the only 100 per cent take (Case 7, Table III) was on a sacral decubitus to which only boric compresses were applied. In a bilateral granulating burn of the legs (Case 4, Table III) although

TABLE III. PENICILLIN IN SKIN GRAFTING

PATIENT NO.	AREA GRAFTED	GRAFT	TREATMENT	RESULTING "TAKE" (PER CENT)
1	Granulating burn, hand	Thiersch	Penicillin jelly	70
1	Granulating burn, temple	Thiersch	Penicillin jelly	95
1	Granulating burn, leg	Thiersch	Penicillin jelly	95
2	Granulating burn, leg	Dermatome	Penicillin jelly	50
3	Granulating burn, leg	Dermatome	Penicillin jelly 120,000 U. a day parenteral	45
4	Granulating burn, leg	Dermatome	Penicillin compress	90
4	Granulating burn, leg	Dermatome	Boric compress (no penicillin)	90
5	Granulating wound, leg	Dermatome	Penicillin jelly 200,000 U. a day parenteral	75
6	Granulating wound, back	Dermatome	Penicillin compress	0
7	Sacral decubitus	Dermatome	Boric compress (no penicillin)	100
8	Sacral decubitus	Dermatome	Penicillin compress	0
8	Sacral decubitus	Dermatome	Penicillin 200,000 U. a day parenteral	0
9	Sacral decubitus	Dermatome	Penicillin 200,000 U. a day	80

the degree of take was equal on the penicillin and control side, the latter showed the smoother, better graft. The graft on the decubitus (Case 8, Table III) failed completely, both when local and when parenteral penicillin was used.

Two recently observed patients not in this series showed little benefit from penicillin.

CASE 1.—A soldier with granulating burns of chest and thigh received a dermatome graft to the thigh while on 200,000 units penicillin a day, with 70 per cent take. A few days later, while receiving only an occasional local dressing of penicillin jelly, the lesion of the chest was grafted with 60 per cent take.

CASE 2.—An officer with a large granulating shell fragment wound of the thigh received first a dermatome graft while getting no medication. The graft was 40 per cent successful. A few days later, while receiving penicillin both locally in saline compresses and parenterally in daily doses of 160,000 units, his wound was regrafted with complete failure.

From these few cases it would appear that in such wounds where infection is at a minimum, and where much of the flora is resistant to penicillin, metabolic factors and technical details play the dominant role and that the drug adds little to the chance of success of the graft. Hirshfeld and co-workers,<sup>14</sup> however, were enthusiastic over the benefit of parenteral penicillin in a series of nineteen skin grafts.

To conclude, penicillin is indisputably of paramount value in the surgery of contaminated wounds. This is being eloquently proved by our forward surgeons<sup>15, 16</sup> in the theaters of war. It is indicated, but less convincingly so,

in very long operations where asepsis cannot be made absolutely ideal, and in secondary wound closure. In skin grafting and primary closure of pilonidal sinus excision wounds its value is still to be proved.

*Penicillin in Bone and Joint Infections.*—

*Osteomyelitis and septic compound fractures:* Our experience consists of eleven cases of staphylococcal hematogenous osteomyelitis and eighteen cases of secondary osteomyelitis and septic compound fractures, also predominantly staphylococcal, as summarized in Tables IV and V, respectively. These few

TABLE IV. PENICILLIN IN HEMATOGENOUS OSTEOMYELITIS

CASE NO.	AGE	DESCRIPTION	TREATMENT	RESULTS
1	4 mo.	Osteo.* of humerus with staphylococemia	Parent.† 443,000 U. in 30 days; drainage of soft tissue abscess	Inactive by 56th day; involucrum formed
2	11 yr.	Osteo. of upper tibia	Parent. 1,640,000 U. in 10 days + local; drainage and drilling of bone	Sinus persists after 247 days; sequestration
3	37 yr.	Flare-up of old osteo., lower femur	Parent. 4,359,000 U. in 36 days + local; wide drainage and curettement of bone	Healed with excellent function 47th day
4	19 yr.	Osteo. of tarsals of foot	Parent. 3,200,000 U. in 31 days; incision and drainage of soft tissues	Healed without sequestration 63rd day
5	22 yr.	Osteo. of upper femur and arthritis, hip joint	Parent. 9,610,000 U. in 52 days + one 10,000 U. local injection; no surgery	Healed with normal joint motion 90th day
6	22 yr.	Osteo. of upper femur and arthritis, hip joint	Parent. 10,145,000 U. in 33 days; late in disease abscess of hip drained	Joint destroyed; still draining after 1½ yr.
7	30 yr.	Old Brodie's abscess of femur with sinus	Parent. 2,310,000 U. in 19 days; extraction of small sequestrum and curettement	Healed 17 days after removal of sequestrum
8	25 yr.	Osteo. of radius with sequestration	Parent. 8,250,000 U. in 55 days; saucerization and primary wound closure	Wound healed per primam
8	25 yr.	Osteo. of ilium (same patient as above)	Parent. 8,250,000 U. in 55 days; sequestrectomy	Wound healed by 43rd day
9	35 yr.	Osteo. of ilium and sacroiliac joint	Parent. 10,350,000 U. in 79 days after local penicillin failed; sequestrectomy	Wound healed by 150th day
10	29 yr.	Osteo. of ilium and sacroiliac joint	Parent. 11,300,000 U. in 56 days + local, sequestrectomy	Wound healed by 89th day

\*Osteo., osteomyelitis..

†Parent., parenteral.

cases raise some interesting questions. The characteristically rapid relief of pain in these cases was well demonstrated in patients (Case 5, Table IV, and Cases 4 and 6, Table V) who were relieved of their suffering in twenty-four, forty-eight, and nine hours, respectively. The first two of these patients had been unimproved by adequate sulfadiazine therapy.

In Cases 2 and 7, Table IV, and Cases 2 and 3, Table V, penicillin showed no superiority to what might be expected of the sulfonamides. In all other instances it showed definite superiority to the results obtained or to those

TABLE V. PENICILLIN IN SECONDARY OSTEOMYELITIS AND SEPTIC COMPOUND FRACTURES

CASE NO.	AGE (YR.)	DESCRIPTION	TREATMENT	RESULT
1	25	Infected compound fracture of upper femur	Parent.* 9,660,000 U. in 86 days + local; wound explored 3 times	Healing 94th day after removal of fragments
2	30	Fracture, neck of femur, with infected bone graft	Parent. 6,170,000 U. in 56 days + local; incised and drained once	Wound continued to drain
3	23	Infected compound fracture of upper femur	Parent. 2,520,000 U. in 22 days; exploration and drainage of wound	Drainage continued; leg amputated
4	26	Infected amputation stump, leg; periostitis, tibia	Parent. 4,050,000 U. in 25 days; later reamputated 2 in. higher	Infection controlled; slight drainage persisted
5	28	Infected amputation stump, leg; periostitis, tibia	Parent. 6,135,000 U. in 31 days; no surgery	Healed in 40 days in spite of poor blood supply
6	21	Infected amputation stump, leg, with 4 cm. bare tibia	Parent. 6,895,000 U. in 34 days; excision $\frac{1}{4}$ in. of tip of tibia	Nearly healed 34th day when transferred
7	23	Infected, severely lacerated compound fracture of fibula†	Parent. 7,725,000 U. in 55 days + local; no surgery	Soft tissue wound healed 67th day
8	33	Low-grade anaerobic infection bone graft, tibia‡	Parent. 6,430,000 U. in 20 days; no surgery	Slow subsidence after sulfonamide therapy had failed
9	29	Septic compound fracture of humerus and glenoid process	Parent. 3,675,000 U. in 36 days + local; excision of head and neck of humerus	Smooth P.O. course; healed 36th day
10	27	Infected inlay bone graft for nonunion, ulna	Parent. 2,611,000 U. in 14 days; no surgery	Graft saved; wound healed by 14th day
11	30	Osteo.,§ iliac crest, from gunshot wound	Parent. 6,697,000 U. in 46 days + local; sequestrectomy	Wound healing complete 46th day
12	32	Osteo., head 2nd metatarsal from nail puncture	Parent. 3,720,000 U. in 24 days; no surgery required	Infection resolved; function restored
13	22	Osteo., postoperative, lamina lumbar 4	Parent. 4,775,000 U. in 36 days; early sequestrectomy	Sound healing 41st day
14	25	Osteo., postoperative, laminae lumbar 4 and 5	Parent. 350,000 U. in 15 days (inadequate); no sequestrectomy	Prolonged drainage; healing about 140th day
15	20	Osteo., skull secondary to frontal sinusitis; brain abscess	Parent. 15,730,500 U. in 99 days + local; sequestrectomy later	Wound healed 37th day (14th day P.O.)
16	44	Osteo., left mandible, early, and severe cellulitis of face	Parent. 5,270,000 U. in 50 days; drainage of submandibular abscess	Rapid control of cellulitis; early osteo. aborted
17	39	Osteo. of maxilla with multiple small sequestra	Parent. 2,250,000 U. in 18 days; removal of several small sequestra	Gums healed 37th day
18	25	Osteo. of ascending ramus of mandible	Parent. 4,625,000 U. in 44 days; intraoral curettement of ramus	Steady progress to complete destruction, ramus

\*Parent., parenteral.

†Culture included *Cl. welchii* without clinical gas gangrene.‡Organisms isolated at first (but not at second) aspiration: *Cl. sporogenes* and *Cl. aerofetidum*.

§Osteo., osteomyelitis.

which might have been expected to the sulfonamide drugs. In Cases 4 and 5, Table IV, and Cases 5, 10, 12 and 15, Table V, penicillin proved brilliantly successful after sulfadiazine had failed.

The following cases demonstrate what may be accomplished by penicillin.

CASE 5 (Table IV).—A 22-year-old white sergeant with early osteomyelitis of the left upper femur and septic arthritis of the hip joint, at first undiagnosed, was treated from September 26 to October 12, 1943, on oral sulfadiazine. Upon arrival at Walter Reed General Hospital his temperature was spiking to 103° and 104° F.; he was acutely ill and in great pain, holding his left thigh rigidly flexed and internally rotated. Seven cubic centimeters of thick pus culturing hemolytic *Staph. albus*, coagulase positive and sensitive to 0.4 units penicillin, were aspirated and 10,000 units penicillin injected in 10 c.c. normal saline solution. At the same time intramuscular injections of 30,000 units every three hours and dicoumarin therapy were instituted, traction being applied to the lower extremity over Buck's extension. Within twenty-four hours there was marked relief of pain and progressive improvement followed. Penicillin was discontinued Dec. 3, 1943, and by Jan. 12, 1944, the soldier was allowed up and around on crutches. When last seen, March 3, 1944, three months after cessation of penicillin, he was free of symptoms and had perfect range of hip motion. Roentgenograms, which had shown progressive bone destruction of the upper femur up to mid-November, 1943, by this time showed considerable healing and new bone formation.

CASE 12 (Table V).—A 32-year-old Norwegian commando instructor stepped on a nail June 2, 1943, developing low-grade osteomyelitis of the left second metatarsal as proved by x-ray picture. There was swelling, pain, and low spiking fever failing to respond to sixteen days of intensive sulfadiazine with blood levels 12 to 14 mg. per cent. His foot was immobilized in plaster and he received penicillin therapy as shown in Table V. When last seen Aug. 16, 1943, he was taking ten-mile hikes and x-ray views showed arrest of the destructive bone process without evidence of sequestration.

CASES 6 AND 10 (Table V).—The first patient, with a badly infected (beta hemolytic streptococcus and *Staph. aureus*) lower leg amputation stump, the second with an infected inlay bone graft for nonunion of the ulna, culturing hemolytic *Staph. aureus*, presented the serious problem of rough denuded bone and badly infected soft tissues. In addition, in Case 10 it was feared that the bone graft with its metal fixation screws would fail. Under penicillin therapy, the patient healed completely in fourteen days and the graft was saved. In Case 6, after one-quarter of an inch of the tibial tip was excised, granulation tissue rapidly closed over the remaining bare bone. The stump was practically healed when the patient was transferred to another hospital thirty-four days after the start of treatment.

That penicillin can prevent sequestration in acute osteomyelitis and obviate radical surgical intervention is demonstrated by Cases 4 and 5, Table IV, and Cases 12 and 16, Table V. Drainage of soft tissue abscess was necessary in Case 4, Table IV, and Case 16, Table V. In the remaining seven patients (Cases 1, 2, 6, 8, and 10, Table IV and Cases 15 and 17, Table V) with acute osteomyelitis, sequestration occurred and surgical intervention of varying magnitudes was necessary. Thus (Case 2, Table IV), a young girl, receiving early and vigorous treatment (200,000 units daily) proceeded to sequestration and sinus formation. Possibly a much larger initial dosage, longer continued therapy, and repeated aspiration of pus instead of the more destructive surgery might have succeeded better.

The outcome in any of these cases was unpredictable at the outset because it depended upon the fate of the blood supply to the infected bone. We have lately become impressed with the unexpected success achieved by greatly in-

creased dosages, and wonder if early osteomyelitis might not be more often arrested if huge amounts of penicillin were given initially in the attempt to get an effective quantity of the drug across the barrier of thrombosing arterioles and capillaries where a lower blood level would fail. Concomitant anticoagulant therapy has not been satisfactorily investigated. What share the dicoumarin had in the remarkable result obtained in Case 5, Table IV, we cannot say.

Probably the least satisfactory response of all bone suppurations is the septic compound fracture of the femur. There were two failures among the three wounds of this type (Cases 1, 2, and 3, Table V). The explanation may possibly lie in the large muscle mass surrounding the bone capable of hiding sequestra and rendering drainage difficult. Thus, in Case 1 drainage persisted a long time and not until the third exploration was a pocket discovered, harboring numerous small necrotic bone fragments. Healing occurred soon thereafter.

As to osteomyelitis of the skull and pelvis (see Cases 8, 9, and 10, Table IV, and Cases 11 and 15, Table V), in no instance was healing achieved without surgical removal of necrotic bone. However, a single sequestrectomy together with penicillin was followed by healing in all cases. It is noteworthy that in Case 9, Table IV, in spite of twenty aspirations of pus with local injection each time of 10,000 to 25,000 units penicillin along with parenteral therapy, the process continued to advance until radical surgery was resorted to.

Our experience with primary closure of soft tissues following sequestrectomy in subacute and chronic osteomyelitis is limited to a single but satisfactory instance, Case 8, Table IV. However, wherever the soft tissues permit of closure without tension and dead space, this would appear to be a feasible procedure.

In chronic osteomyelitis we have several times observed, as have others,<sup>17, 18</sup> that even though the drainage may become temporarily sterile under penicillin, at operation staphylococci may still be cultured from the depths of the involved bone and sclerotic tissues where they have evidently been sealed away beyond the reach of the blood borne or locally instilled agent. These mechanical and vascular factors explain the difficulty of treating chronic skeletal infections and also their unpredictable recurrences.

*Septic arthritis:* Of our small group of five cases of septic arthritis only one patient had complete recovery and one partial. These two (Cases 1 and 5, to be discussed) received penicillin locally whereas the other three did not. Although about 50 per cent of the circulating drug crosses the synovial membrane<sup>7</sup> it is well to supplement parenteral with local injections of penicillin. Brief descriptions of the cases follow.

(1) CASE 5 (Table IV, previously described in detail).—A patient with osteomyelitis of the upper left femur and septic arthritis of the hip joint had complete restoration of hip motion following a single local injection of 10,000 units of penicillin and intramuscular injections totaling 9,650,000 units.

(2) CASE 6 (Table IV).—A patient with a lesion closely similar to that of the patient in Case 5 received 10,145,000 units intramuscularly and none locally. Complete destruction of the hip joint and a persistently draining sinus resulted.

(3) A postoperative staphylococcal suppuration of the knee joint following an open reduction of a fractured tibial condyle was widely drained. The patient received 4,075,000 units parenterally but none locally. The severe general sepsis was easily overcome but the knee ankylosed.

(4) A patient with mixed streptococcal and staphylococcal arthritis of the proximal joint, index finger, following a laceration that entered the joint, received 3,800,000 units parenteral penicillin but ended with amputation of the finger.

(5) A patient with staphylococcal suppuration of the fifth metacarpophalangeal joint, likewise of traumatic origin, was treated by local instillations through a ureteral catheter as well as by 2,400,000 units of parenteral penicillin. Healing followed but with a rather stiff, swollen, somewhat painful joint.

*Penicillin in the Treatment of Burns.*—Our experience with penicillin in burns consists in the seven cases shown in Table VI and in a few later cases not included in this report.

TABLE VI. PENICILLIN IN THE TREATMENT OF BURNS

CASE NO.	AGE (YR.)	DESCRIPTION OF BURN (LOCATION, PER CENT BODY SURFACE INVOLVED, DEPTH, DURATION)	PENICILLIN TREATMENT	RESULTS
1	28	Hand; about $\frac{1}{2}\%$ ; 2nd degree; 8 hr. old	Local in aquafor	Healed 10th day; no clinical infection
2	22	Face, head, hands, legs; total 15%; 2nd & 3rd degree; 12 days old	Local in tragacanth jelly	Healed, with grafting on 46th day
3	29	Thighs, legs; total 7%; chiefly 3rd degree; 120 days old	Local in tragacanth jelly	Healed with grafting on 46th day
4	55	Rt. arm, thigh, leg and perineum; total 13%; 2nd and 3rd degree; 36 hr. old	Parent.* 5,424,000 U. in 44 days; local in aquafor	Probably saved life; nearly healed 70th day
5	25	Neck, shoulder, arm; total 5%; 3rd degree, infected; 160 days old	Local in tragacanth jelly	Checked infection when sulfonamide failed
6	26	Face, head, forearms; total 22%; 2nd and 3rd degree; 36 hours old	Parent. 2,050,000 U. in 11 days; no local	Died 11th day; cause undetermined
7	23	Thighs and legs; total 18%; 3rd degree; 60 days old	Parent. 3,480,000 U. in 28 days; local in aquafor	Died 28th day; cause undetermined

\*Parent., parenteral.

In the fresh extensive burn such as Case 4, Table VI, parenteral penicillin as a prophylaxis against infection should supplant the sulfonamides since it is more potent against streptococci and staphylococci and has none of their untoward side effects. The aforementioned patient, extremely obese, hypertensive, and possessing an enormous ventral hernia had a relatively smooth course, never developing sepsis in the deep second degree burns.

Penicillin applied locally in a water-soluble base (200 to 250 units per cubic centimeter) is a very satisfactory dressing for minor burns such as were found in Case 1, Table VI. We have also used the local application for the sloughing and granulating stage of third degree burns prior to skin grafting as in Cases 2 and 3, Table VI. When these lesions are relatively clean and harbor only the inevitable staphylococci of low pathogenicity and high resist-



creased dosages, and wonder if early osteomyelitis might not be more often arrested if huge amounts of penicillin were given initially in the attempt to get an effective quantity of the drug across the barrier of thrombosing arterioles and capillaries where a lower blood level would fail. Concomitant anticoagulant therapy has not been satisfactorily investigated. What share the dicoumarin had in the remarkable result obtained in Case 5, Table IV, we cannot say.

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TABLE VII. PENICILLIN IN CENTRAL NERVOUS SYSTEM SEPSIS

CASE NO.	AGE (YR.)	DIAGNOSIS	CULTURE	TREATMENT	RESULT
1	20	Pansinusitis, frontal osteomyelitis, frontal lobe abscess	Staph. aureus; anaerobic hem. Str.	Parent.* 15,355,000 U. in 99 days + local 375,000 U.; surgery to skull and abscess	Complete recovery 127th day; returned to duty
2	23	Cerebellar abscess secondary to lung abscess	Nonhem. Str.	Parent. 14,360,000 U. in 53 days, local 75,000 U.; drainage of abscess	Recovery 53rd day; lung abscess also quiescent
3	27	Postoperative temporal lobe abscess and meningitis	Abscess and spinal fluid; Staph. aureus	Parent. 3,287,000 U. in 14 days, local 107,000 U.; drainage of abscess	Recovered and discharged home 32nd day
4	22	Frontal lobe abscess from fracture of cribriform plate	Staph. aureus; non-hem. Str.	Parent. 5,295,000 U. in 36 days, local 25,000 U.; drainage of abscess	Developed brain fungus; recovery delayed to 200th day
5	23	Large epidural abscess, etiology obscure	Hem. Staph. aureus sensitive to 4.0 U.	Parent. 7,650,000 U. in 36 days + local; laminectomy, later secondary closure	Ambulatory 41st day; returned to duty 165th day
6	38	Postoperative epidural abscess covering entire lumbar cord	Beta hem. Str. sensitive to .0025 U.	Parent. 2,060,000 U. in 13 days + local; no surgery	Decompression obviated; healed 20th day; duty
7	22	P.O. osteomyelitis 4th lumbar lamina and epidural abscess	Hem. Staph. aureus sensitive to .0078 U.	Parent. 4,775,000 U. in 36 days; sequestrectomy at outset	Healing complete 41st day; returned to duty 125th day
8	25	P.O. osteomyelitis 4th lumbar lamina and epidural abscess	Staph. aureus; Staph. albus	Parent. 45,000 U. in 15 days; no local, no sequestrectomy	Final healing not till 140th day; returned to duty 172nd day
9	22	Meningitis from basilar skull fracture into frontal sinus	Staph. aureus coagulase positive	Intrathecal and later intraventricular; total 112,500 U., no parenteral	Sulfonamide failure; intraventricular better than intrathecal; survived
10	47	Late, neglected meningococcus meningitis	Probable meningococcus	Parent. 2,046,000 U. in 9 days; local 120,000 U., intrathecal and cysternal	Never completely conscious; died 11th day
11	5	Purulent meningitis	Organism unidentified	Parent. 1,585,000 U. in 40 days; local 197,000 U.	Recovered
12	22	Acute mastoiditis, septicemia, meningitis	Beta hem. Str. throughout	Parent. 625,000 U. in 3 days, no local; mastoidectomy night of entry	Died 2nd day of pulmonary edema in spite of sterilized blood and spinal fluid

\*Parent., parenteral.

TABLE VIII. PENICILLIN IN

CASE NO.	AGE (YR.)	DIAGNOSIS	BACTERIOLOGIST
1	27	Empyema formed while getting penicillin for pneumonia	Pneumococcus Type I; susceptible to .0025 U.
2	21	Empyema, left, coincident with pneumonia	Staph. aureus, susceptible to .35 U.
3	18	Empyema, left, complicating lobar pneumonia, left	Hem. Staph. aureus, susceptible to .04 U.
4	35	Empyema, left complicating pneumonia	Beta hem. Str.
5	30	Empyema, right, complicating pneumonia	Beta hem. Str.
6	36	Empyema, left, complicating pneumonia	Beta hem. Str.
7	18	Empyema, right, complicating pneumonia	Beta hem. Str.
8	26	Empyema, left, complicating atypical pneumonia	Hem. Staph. aureus
9	37	Empyema, left, following lobar pneumonia	Pneumococcus Type V; susceptible to .02 U.
10	20	Bronchiectasis, left lower lobe, with secondary pyopneumothorax	Nonhem. Str.; Staph. albus and mixture
11	29	Lung abscess, left upper lobe, 4 weeks' duration	Mixed flora; no predominant organisms
12	40	Lung abscess, left upper lobe, 9 weeks' duration	Predominant, alpha Str. mitis
13	25	Acute lung abscess, right upper followed by same in right lower	Predominant, alpha Str. salivarius
14	43	Multiple lung abscesses, right upper lobe, 4 mo. duration	Alpha Str. of 2 varieties
15	35	Lung abscess, right upper, with much pneumonitis, 5½ mo.	Chiefly alpha Str.; few Beta Str.
16	23	Multiple lung abscesses, left upper, 3 mo. duration; secondary brain abscess	Alpha hem. Str. salivarius
17	24	Lung abscess, left lower lobe, 4 mo. duration	Alpha Str.; at times Beta Str.
18	27	Lung abscess, multiple, right upper lobe, 6 mo. duration	Alpha and Beta Str.; at times Staph.
19	30	Infected cyst left lower lobe simulating abscess, 4 mo.	Alpha Str.; non-hem. Str.
20	24	Putrid empyema, P.O., from lobectomy for chronic lung abscess	Str. faecalis; diphtheroids
21	22	Lung abscess, right upper, 8 mo. duration	Abscess; Beta hem. Str., empyema, no growth
19	30	Putrid empyema, early, following lobectomy (same as Case 17)	Hem. Staph. albus; hem. influenzae
18	27	Lung abscess, multiple, right upper lobe, 12 mo. duration	Alpha hem. Str. and a mixture
22	40	Bronchiectasis, left lower lobe with large cyst formation, 9 mo.	Alpha hem. Str.
10	20	Case 10 above, cystic bronchiectasis, after healing of empyema	None obtained

Note: Three patients in this group (Cases 10, 18, and 19) appear twice, since they each represent two distinct applications of penicillin therapy with an interval between.

\*Parent, parenteral.

## SURGICAL CHEST CONDITIONS

TREATMENT	RESULTS
Parent.* 1,650,000 U. in 14 days, no local; drug stopped, rib resected	Empyema cured 21 days after rib resection
Parent. 3,510,000 U. in 18 days, no local; rib resection 7th day of drug	No improvement until rib resection, then rapid
Parent. 7,500,000 U. in 6 days, local 290,000 U. 6 taps; rib resection	No improvement until rib resection, then rapid
Parent. 17,550,000 U. in 90 days, local 380,000 U. 12 taps; rib resection	No improvement until rib resection, then slow
Parent. 1,790,000 U. in 12 days, local 120,000 U. 10 taps; rib resection	No improvement until rib resection
Parent. 11,883,000 U. in 60 days, local 390,000 U. 11 taps; closed, then open drainage	Unimproved until rib resection
Parent. 17,405,000 U. in 84 days, local 75,000 U. 3 taps; rib resection	Unimproved until rib resection
Parent. 12,600,000 U. in 65 days, local 100,000 U. 2 taps; rib resection	Little improvement until rib resection
Parent. 1,775,000 U. in 16 days, local 160,000 U. 8 taps; rib resection	Little benefit until rib resection
Parent. 5,280,000 U. in 38 days; closed thoracotomy	After sulfonamides failed, healed on penicillin
Parent. 6,400,000 U. in 33 days; sulfonamide (blood level 13) without benefit	Prompt improvement, clinical cure within 1 mo.
Parent. 4,545,000 U. in 31 days; beginning to improve even before penicillin	Rapid regression to clinical cure
Parent. 4,915,000 U. in two courses, 19 and 7 days respectively	First abscess cured; 2nd abscess rapidly resolving
Parent. 4,800,000 U. in 39 days; had been considered malignancy	Dramatic and rapid clinical cure
Parent. 10,445,000 U. in 34 days; was being prepared for lobectomy	Rapid subsidence of fever and sputum to normal; arrested
Parent. 14,360,000 U. in 53 days (same patient as Case 2, Table VII)	Still asymptomatic after 6 mo.; small cavities still seen by x-ray
Parent. 4,402,000 U. in 28 days; pneumothorax from 1st stage drainage	No significant benefit; cured following pneumothorax
Parent. 9,165,000 U. in 38 days; 2 stage drainage, inadequate	No benefit; went to lobectomy (see below)
Parent. 10,020,000 U. in 51 days; 1st stage drainage of abscess	Some reduction in sputum, no change in x-ray picture
Parent. 5,885,000 U. in 30 days; rib resection 4 days before starting drug	Probably saved patient's life; returned to limited duty
Parent. 11,275,000 U. in 58 days; lobectomy and later rib resection for empyema	Developed putrid empyema, but recovered
Parent. 7,700,000 U. in 40 days; thoracotomy three times	Recovery with good re-expansion left upper lobe
Parent. 7,435,000 U. in 47 days, local 50,000 U.; lobectomy and later thoracotomy	Developed putrid empyema but recovered
Parent. 5,825,000 U. in 30 days; lobectomy after 20 days conservatism	Per primam healing of wound and uneventful recovery
Parent. 3,400,000 U. in 12 days, local 100,000; lobectomy, left lower lobe	Well into convalescence; had minimal empyema

little progress, other than a feeling of increased well-being, was made until rib resection. Of the larger series only three escaped surgery. At another hospital one of these patients was given penicillin at three-hour intervals for four months as the alternative to rib resection. The other two did not appear to have true empyemas in that only thin fluid containing streptococci was yielded. It will be observed that one patient (Case 1) developed empyema while receiving penicillin for Type I lobar pneumonia; yet rapid healing followed rib resection after stopping the drug. Although it is not shown in Table VIII, one patient (Case 6) failed to make satisfactory progress on penicillin plus a poorly draining closed thoracotomy. Prompt response followed rib resection. Likewise, patients (Cases 4 and 8) with rib resections done and receiving 200,000 units penicillin daily experienced temporary flare-ups when drainage became partly blocked and then returned to normal when this was corrected. In five cases, or 50 per cent, although the empyema was promptly sterilized on local and parenteral injections, pus continued to form and at rib resection 1,000 to 2,000 c.c. were evacuated. Our observations in this and in the larger series seem to show that penicillin is useful in empyema in controlling early systemic infection or accompanying pneumonia. However, if pus continues to form and is not satisfactorily decreasing within ten to fourteen days on parenteral and local penicillin and repeated aspirations, rib resection should be done without further delay, if mediastinal stabilization is adequate. Every effort should, of course, be made to diagnose empyema in its earliest phase when there will be reasonable likelihood of aborting the process by parenteral and local penicillin injections together with repeated aspirations.

A preliminary controlled study was also made of the effect of parenteral penicillin upon the final healing of empyema following rib resection. Four patients were placed upon parenteral penicillin (25,000 units intramuscularly every three hours) from the time of operation until their cavities had shrunk to less than 10 c.c. capacity and the tubes were removed. Five comparable and unselected patients, during the same season (February to June, 1944), receiving no penicillin, served as controls. The only other difference in the management of the two groups was that the test patients, kept on the penicillin ward, received an unusually high protein and vitamin diet and in addition averaged 2,000 c.c. of blood and 350 c.c. of plasma each during the study period, while only one blood transfusion was given to the entire control group. With exception of one penicillin-treated patient, however, whose red cells numbered 3,850,000 and hemoglobin 70 per cent, all patients of both groups had red counts over 4,100,000 and hemoglobin values of 80 to 85 per cent. Cultures of three test cases revealed beta hemolytic streptococcus and one pneumococcus; of the controls, one cultured pneumococcus, two beta hemolytic streptococcus, and one probable beta hemolytic streptococcus and one alpha hemolytic streptococcus. The comparable data are shown here:

	AVERAGE DURATION UNTIL THORACOTOMY (DAYS)	AVERAGE INITIAL SIZE OF CAVITY (C.C.)	AVERAGE DAYS UNTIL TUBE OUT
Penicillin cases	44	1625	119
Control cases	41	1300	156

Clinically the only noticeable difference between the experimental and control cases was a definite reduction in the growth of granulation tissue around the drainage tube in the penicillin cases. Trimming or cauterizing of these excess granulations was repeatedly necessary in the control patients but only once in a test patient. This inhibition of granuloplasia by the agent we have noticed elsewhere and Florey and Williams<sup>21</sup> have observed it in penicillin-treated infections of the hand. The lessening of morbidity shown in this small series is perhaps suggestive enough to warrant further study. However, until practical methods are worked out of maintaining effective penicillin levels by fewer injections, the lessened healing time will scarcely justify the prolonged needling of the patient.

*Lung abscess without lobectomy* (Cases 11 through 19, Table VIII): The deciding factor as to cure in cases of lung abscess without lobectomy seemed to be the degree of thickening and noncollapsibility of the cavity wall. Nor was this predictable entirely upon the duration of the lesion since two of the most responsive patients (Cases 14 and 15, Table VIII) had had symptoms for four and five and one-half months, respectively. It is our impression that penicillin is definitely superior to the sulfonamides in treating lung abscess and that relatively early and not too large abscesses will yield to the new drug in the great majority of cases without drainage. An interesting situation developed in several cases, notably 12, 14, 15, and 16, Table VIII, in which there was clinical cure but persistence of small nonactive cavities by x-ray. A soldier (Case 15) was being prepared for lobectomy but progressed so favorably on penicillin that he was, instead, sent out to limited duty for six months. It is too early to predict what the outcome will be in such lesions. The flora in nearly all the abscesses, for the most part obtained at bronchoscopy, was a mixture usually with alpha hemolytic streptococcus predominant. This culture usually persisted throughout regardless of the clinical course of the patient. Undoubtedly anaerobes were sometimes present in the abscesses and certainly in the putrid empyemas, although not detected by us.

*Lung abscess with lobectomy*: Of the 4 patients with lung abscess with lobectomy (Cases 18, 19, 20, and 21, Table VIII), two (Cases 18 and 19) had received thirty-seven and fifty-one days of intensive penicillin therapy before lobectomy with no significant improvement. One (Case 18) had had in addition, a two-stage drainage of the main abscess. Although the other (Case 19) proved to have an infected cyst, the surgical problem of its removal was similar to that presented by a chronic lung abscess. Penicillin was started in two instances (Cases 19 and 20) after lobectomy and as empyema was developing. In the other two (Cases 18 and 21) it was initiated nineteen and one days, respectively, before operation. Putrid empyema developed in all four cases but the patients survived. These four consecutive survivals, although of no statistical significance, are clinically important especially when it is realized that in the past lobectomy for chronic lung abscess carried a mortality in the neighborhood of 50 per cent.

*Bronchiectasis with lobectomy*: One patient (Case 10, Table IX) was saved by penicillin from a probable fatality following the development of pyopneumo-

thorax after sulfonamides had been unavailing. But the drug had no significant effect upon his underlying bronchiectasis. Nor did several weeks of treatment influence the bronchiectasis in Case 22. This is just as one might expect, considering the anatomic basis of the disease. Therefore, both patients were subjected to lobectomy under protection of heavy penicillin dosage. Both healed without developing empyema.

*Penicillin in Intrathoracic "Medical" Disease.—*

*Pneumococcus lobar pneumonia:* Six patients with pneumococcus pneumonia were treated with doses varying from 390,000 to 1,650,000 units. The duration of infection prior to penicillin ranged from one to six days with an average of three days. Three patients had shown no improvement despite adequate sulfadiazine therapy. Temperature returned to normal in from twelve to seventy-two hours (average thirty-six hours) following institution of penicillin therapy. In three cases sputum was sterile on culture as early as twenty-four hours after penicillin was begun. Blood cultures remained sterile in all cases. No complicating empyemas occurred. Larger doses than are ordinarily employed were considered necessary in the majority of these patients because of the duration of the infection prior to treatment or the absence of response to sulfadiazine. Tillet, Cambier, and McCormack<sup>22</sup> have worked out to a nicety the minimum dosage and treatment days required to cure lobar pneumonia.

*Acute staphylococcal pulmonary infections:* With the exception of one patient (Case 8, Table IX) all the members of the group with staphylococcal infections were exceedingly toxic and desperately ill (in fact one, Case 11, was moribund) when penicillin was started. In all cases sulfonamides had either failed or were producing no clinical improvement. Penicillin undoubtedly saved the lives of three patients (Cases 7, 9, and 10) and probably one other also (Case 8). In two (Cases 7 and 8) the temperature returned to normal within seventy-two hours and the clinical improvement was phenomenal.

When penicillin was started in one patient (Case 10, Table IX) he presented patchy consolidation of the entire right lung and a serosanguineous pleural effusion. Under therapy, temperature returned to normal on the twentieth day and all parenchymal lesions passed through the stage of multiple small cavities to complete disappearance to x-ray. The pleural effusion after temporarily loculating was reabsorbed, and did not become infected (fluid penicillin level 0.078 Oxford units). A patient (Case 11) treated at another hospital, under our direction, might possibly have been saved if penicillin had been started earlier.

*Streptococcal pulmonary infections:* The latter two of the three cases are presented in some detail.

CASE 13 (Table IX).—The patient was growing more critically ill in spite of adequate sulfadiazine therapy, and presented the picture of *overwhelming generalized sepsis*: bilateral bronchopneumonia, septicemia, widespread erythematous and hemorrhagic manifestations, left pleural effusion, and physical and electrocardiographic evidence of pericarditis with effusion. Forty-eight hours after the start of penicillin there was remarkable im-

provement and by the tenth day the temperature had dropped from 105.5 to 99.0° F. Within this time the right lung had completely cleared, though some pneumonitis may well have persisted within the left lung, obscured and compressed by the pleural effusion. Characteristically the left pleural effusion, although culturally sterile throughout, developed into empyema with high spiking fever, in spite of vigorous parenteral therapy and two 40,000 unit local injections. Final subsidence of fever and infection was much delayed even after rib resection and continued parenteral penicillin. The reason for this was never discovered.

CASE 14 (Table IX).—This patient was started on treatment twelve hours after the onset of illness. Dysphagia disappeared in twenty-four hours; tonsillar exudate cleared in forty-eight hours. On the fourth treatment day, the patient expectorated large quantities of purulent sputum containing fibrinous bronchial plugs culturing alpha hemolytic streptococci and rapid recovery followed.

*Chronic pulmonary disease:* In both of the patients (Cases 15 and 16, Table IX) with chronic bronchitides, anatomic changes in the bronchial tree had advanced so far that even had all bacteria been destroyed, reinfection would have been inevitable.

*Penicillin in Subacute and Acute Septicemia.*—

*Subacute bacterial endocarditis:* Our own nine-month remission (Case 2, Table X), the apparent success in fifteen out of twenty cases in Dawson and Hunter's series,<sup>23</sup> and the remissions in seven cases reported by Loewe and co-workers<sup>24</sup> bring new hope for cure of subacute bacterial endocarditis.

One patient (Case 1) died of cardiac failure although the blood stream remained sterile during penicillin treatment.

In contrast, another patient (Case 2, Table X) started on the drug the tenth day following the onset of subacute bacterial endocarditis responded very nicely. Blood cultures were sterile twenty-four hours after penicillin was begun, but five days after the completion of a thirty-day course they were again positive. Therapy was then given for an additional sixty-three days intramuscularly and also by the intravenous and subcutaneous drip method. Nine months after therapy there was no evidence of recurrence.

These two cases suggest, first, the importance of early diagnosis and commencement of penicillin treatment, and second, that a relapse after the completion of a month or more of treatment, granted the organism is reasonably penicillin susceptible, demands further trial and perhaps larger dosage of the drug.

*Acute septicemia* (Cases 3 to 13, Table X): Most of the cases of acute septicemia have been presented elsewhere in this paper. The proteus septicemia (Case 12) was treated before a positive blood culture was obtained and is no exception to the known resistance of this organism to penicillin. The only two fatalities among the remaining ten patients (Cases 5 and 11) were practically moribund when penicillin was started.

*Penicillin in Intra-abdominal Suppuration.*—This short and heterogeneous series teaches us little about the effect of penicillin upon these infections. In the desperately ill patients (Cases 1 and 2, Table XI) the drug seemed definitely superior to sulfonamide therapy. This was also true in Cases 6 and 7,



thorax after sulfonamides had been unavailing. But the drug had no significant effect upon his underlying bronchiectasis. Nor did several weeks of treatment influence the bronchiectasis in Case 22. This is just as one might expect, considering the anatomic basis of the disease. Therefore, both patients were subjected to lobectomy under protection of heavy penicillin dosage. Both healed without developing empyema.

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TABLE X. PENICILLIN IN SUBACUTE AND ACUTE SEPTICEMIA

CASE NO.	AGE	DIAGNOSIS	BLOOD CULTURE	PENICILLIN TREATMENT	RESULTS
1	5 yr.	S.B.E.* with patent interventricular septum and aortic insufficiency	<i>Subacute Bacterial Endocarditis</i> Alpha hem. Str., micro-aerophilic, susceptible to .04 U.	2,460,000 U. I.M.† in 32 days	Blood culture sterile after 5 days but again positive when treatment stopped; died of cardiac failure
2	23 yr.	S.B.E. with rheumatic heart disease and aortic insufficiency	Alpha hem. Str. susceptible to .025 U.	18,000,000 U. in 96 days	One relapse after 30 days' therapy; drug restarted; 9 mo. cure, returned to duty
3	27 yr.	Lobar pneumonia, left lower, empyema	<i>Acute Septicemia</i> Pneumococcus, type I	1,650,000 U. I.M. in 14 days	Recovery after drainage of empyema by rib resection
4	29 yr.	Septic pulmonary infarct from furunculosis of auditory canals	Hem. Staph. aureus	1,285,000 U. I.M. in 8 days	Recovered after he had developed osteomyelitis of ilium and sacroiliac joint
5	19 yr.	Bilateral staphylococcal pneumonia	Hem. Staph. aureus	925,000 U. I.M. and I.V.‡ in 4 days	Overwhelmed by the massive lung infection; died
6	18 yr.	Bilateral pneumonia, empyema, left, pericarditis	Alpha hem. Str.	2,830,000 U. parent.,§ 80,000 U. local	Recovery after drainage of empyema by rib resection
7	31 yr.	Primary source unknown	Hem. Staph. aureus	645,000 U. I.V. in 13 days	Blood stream sterilized in 24 hr.; afebrile 9 days after start of treatment
8	24 yr.	Pneumonia, empyema	Str. viridans	2,940,000 U. I.M., 490,000 U. local	Blood stream sterilized in 24 hr.; sulfonamide drugs had failed
9	38 yr.	Cholangitis and liver abscess	Str. viridans	1,965,000 U. I.M. in 27 days	Saved patient's life when sulfonamides had failed
10	4 mo.	Acute ethmoiditis and osteomyelitis left humerus	Hem. Staph. aureus	443,000 U. I.M. in 30 days	Ethmoiditis cleared and osteomyelitis became inactive
11	22 yr.	Acute mastoiditis, and meningitis	Beta hem. Str.	625,000 U. I.M. in 3 days	Blood stream sterilized but developed pulmonary edema; died
12	25 yr.	Old osteomyelitis of left femur	Bacillus proteus	810,000 U. I.M. in 2½ days	Treated before the blood culture report returned; died
13	19 yr.	Osteomyelitis of left upper femur and septic arthritis of hip joint	Hem. Staph. aureus	Parent. 2,460,000 U. in 32 days	Systemic sepsis rapidly controlled but poor result locally

\*S.B.E., subacute bacterial endocarditis.

†I.M., intramuscular.

‡I.V., intravenous.

§Parent., parenteral.

Table XI, two early and large appendiceal abscesses almost constituting localized peritonitis. Both patients had smooth postoperative courses in spite of surgical intervention during the most dangerous period of the disease. These results are encouraging and are in accord with the interesting animal experiments conducted by Fauley and associates,<sup>25</sup> in which they found that appendiceal peritonitis in dogs carrying a 50 per cent mortality when treated by sulfonamides showed 0 mortality when penicillin was started within one hour of the operation and 21 per cent mortality when penicillin was begun twelve hours after the appendix-ligating operation. Regardless of the numerous gram-negative organisms present in appendiceal peritonitis, the streptococci and anaerobes are undoubtedly of chief importance in pathogenesis. In controlling these, penicillin greatly increases the body's defenses. It is not surprising that where fecal leakage persisted, as in Case 4, Table XI, and in two other later cases observed by one of us (J. E. H.), even large doses of penicillin were of no avail.

*Penicillin in Liver Abscess.*—With the exception of the patient (Case 4, Table XII) who was not started on penicillin until exhausted by sixteen days of high fever and sepsis, our results in these few cases are highly encouraging. A patient (Case 2, an early one) receiving only 80,000 units a day would have responded, in our opinion, more promptly to 120,000 to 200,000 units. Case 3 (see penicillin chart, Fig. 6) is here presented in detail.

An 18-year-old soldier, a patient of Lieutenant Colonel J. R. Wells in consultation with us, was admitted to the Station Hospital, Fort McClellan, with a probable localizing appendiceal peritonitis. He grew rapidly worse despite vigorous sulfadiazine therapy and multiple transfusions. When penicillin was finally started, the patient was semistuporous, having five violent chills a day. He was jaundiced and the liver was four fingerbreadths below the costal margin and tender. The spleen was readily palpable. Striking improvement was noted within twelve hours and there was abrupt cessation of chills. Recovery was rapid. A single temperature spike to 103° F. on the tenth penicillin day was thought to be a reaction to a blood transfusion.

*Penicillin in Nonvenereal Genitourinary Infections.*—Genitourinary infections suitable for penicillin therapy and study are uncommon both because the associated mechanical factor usually overshadows the infection, and also because the infecting organisms usually are nonamenable to the drug or are low-grade staphylococci hardly distinguishable from contaminants. The cases presented in Table XIII prove nothing. Even the two patients with sustained symptomatic improvement (Cases 1 and 2, Table XIII) showed no bacteriologic reason for this.

*Penicillin in Dermatologic Infections.*—

*Sycosis vulgaris:* Two patients (Cases 1 and 2, Table XIV) had previously received without benefit practically all known remedies including x-ray and sulfonamides. The first failed to respond to intensive combined local and parenteral penicillin, whereas the second finally responded to prolonged heavy parenteral treatment combined with local applications of penicillin in glycerin. No generalizations can be made here except that prolonged massive dosage may succeed when small or moderate ones fail.

*Deep acne vulgaris*: Cases 3 and 4, Table XIV, demonstrate to our satisfaction that large dosages (up to 45,000 units every three hours) are unavailing against infection superimposed upon a distorted, scarred and cystically-dilated sebaceous apparatus. In these two cases, however, multiple excision of infected cysts and nodules, and primary suture, during administration of parenteral penicillin, resulted in satisfactory per primam healing.

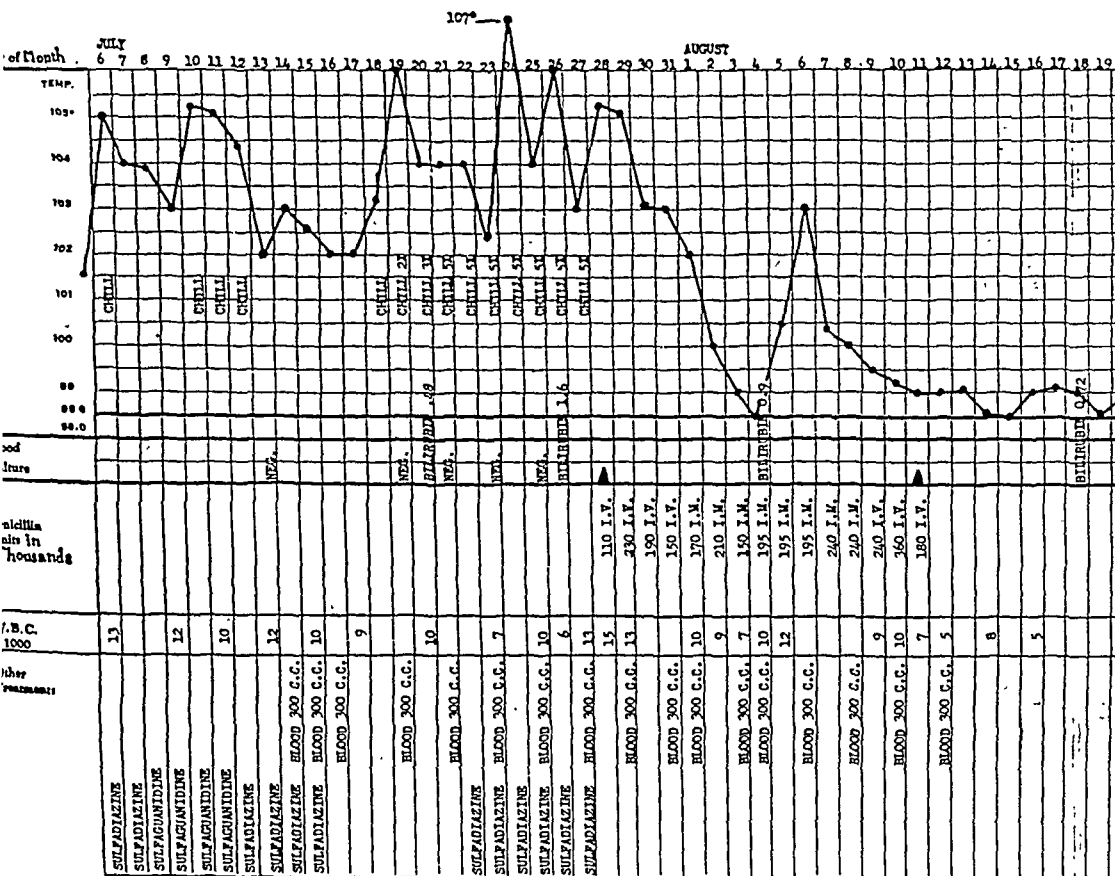


Fig. 6.—Graphic penicillin chart, Case 3, Table XII.

*Pustular bacterid (Andrews)*: In Case 5 appreciable improvement was noted seventy-two hours after institution of penicillin therapy. Improvement obtained after eight days of treatment was equal to that obtained after three weeks of sulfathiazole. The sulfonamide had produced a severe toxic reaction and was therefore no longer available to this patient. Although a longer period of treatment was considered advisable, the patient refused to remain under observation any longer so that final appraisal was not permitted.

#### *Penicillin in Miscellaneous Infections.—*

*Actinomycosis*: We treated two patients with closely similar cases of actinomycosis of the tissues about the angle of the jaw of twenty-nine and twenty-

TABLE XI. PENICILLIN IN INTRAPELITONEAL SUPPURATION

AGE (YR.)	DIAGNOSIS	BACTERIOLOGY	TREATMENT	RESULTS
27	Generalized peritonitis from infected abortion; bronchopneumonia	Str. faecalis; B. coli	Sulfonamide therapy unavailing, parent.* 7,400,000 U. in 36 days; pelvic abscess drained	Apparently lifesaving; afebrile 30th day
47	Generalized peritonitis from ruptured appendix; bronchopneumonia	Initial, alpha hem. Str.	Sulfonamide therapy unavailing, parent. 2,480,000 U. in 14 days; pelvic abscess drained	Rapid localization; afebrile 10th day
34	Generalized peritonitis from ruptured appendix	Gram-positive cocci and aerobacter. aerogenes	Parent. 10,240,000 U. in 43 days; no surgery	Slow recovery; afebrile 35th day
44	Generalized peritonitis from fecal leakage at biopsy site in colon	Lost	Parent. 720,000 U. in 3 days; leak in colon remained unrepai red	Fulminating exitus 5th day
36	Postoperative upper abdominal peritonitis and duodenal obstruction	Beta hem. Str.; hem. Staph. aureus pyogenes	Parent. 1,203,000 U. in 7 days	Died of obstruction but peritoneum sterilized
21	Large early appendic abscess; 5 mo. pregnancy	Esch. coli	Parent. 2,520,000 U. in 7 days, appendectomy on 1th day of disease; local sulfonamide therapy	Rapid recovery; afebrile on 10th day
45	Early appendic abscess; early delirium tremens	Nonhem. Str., Esch. coli, diphtheroids	Parent. 1,500,000 U. in 8 days, appendectomy on 3rd day of disease; local sulfonamide therapy	Rapid recovery; afebrile about 10th day
21	Right subphrenic abscess; right diaphragmatic pleuritis (Cause ?)	Nonhem. Str.; hem. Staph. aureus	Sulfonamide therapy unavailing, parent. 840,000 U. in 14 days; right subphrenic drainage	Apparently lifesaving; afebrile 12th day
31	Retropelitoneal abscess due to fistula from descending colon	B. Friedländer's, Saccharomyces	Sulfonamide therapy unavailing, parent. 1,150,000 U. in 8 days; wide drainage	Died; chemotherapy no effect

\*Parent., parenteral.

TABLE XII. PENICILLIN IN LIVER ABSCESS

AGE (YR.)	DIAGNOSIS	BACTERIOLOGY	TREATMENT	RESULTS
20	Hyperactive amoebic abscess, right lobe of liver, surgically drained	Positive amoebic complement fixation test	11,695,000 U. parenteral, plus local	Rapid subsidence of high temperature;
38	Multiple liver abscesses possibly from cholecystitis	Blood culture once positive for Str. viridans	1,965,000 U. I.M.* in 27 days	No secondary infection, recovered
18	Pylephlebitis secondary to appendiceal abscess	Blood cultures all negative (probably sulfonamide effect)	3,050,000 U. I.M. and I.V.† in 13 days	No response to sulfadiazine (blood levels 19 mg. %) or emetine; penicillin doubtless saved life
48	Multiple abscesses of liver and spleen from appendiceal (?) abscess	Blood cultures sterile; abscess: B. coli, Str., Staph.	1,500,000 U. I.M. in 6 days	Penicillin lifesaving when sulfadiazine had failed

\*I.M., intramuscularly.

†I.V., intravenously.

TABLE XIII. PENICILLIN IN GENITOURINARY INFECTION (NONVENEREAL)

AGE (YR.)	DIAGNOSIS	CULTURE	PENICILLIN TREATMENT	RESULTS
50	Chronic prostatitis of 14 mo. duration	Hem. Staph. albus before and after treatment	250,000 U. in 48 hr.	After sulfadiazine and neoursphenamine failed, still completely relieved 5 mo. after penicillin
52	Chronic prostatitis	Hem. Staph. albus before and after treatment	1,620,000 U. in 12 days	After sulfathiazole and neoursphenamine failed, still completely relieved 7 mo. after penicillin
32	Chronic vesiculitis and prostatitis	B. coli; Str. faecalis; microaerophilic Staph.	4,375,000 U. in 23 days	Temporary relief of symptoms but later recurrence just as with sulfonamides
23	Chronic vesiculitis and prostatitis with acute cystourethritis	Earlier, hem. Staph. albus; at start of treatment, negative	1,935,000 U. in 16 days	Temporary symptomatic relief but pyuria persisted until vasotomy
34	Old rupture of posterior urethra, incontinence, urethritis	Mostly negative; occasional Staph. and diphtheroids	2,175,000 U. in 12 days	No clinical or bacteriologic change
?	Chronic anterior urethritis	Hem. Staph.; nonhem. Str.	2,160,000 U. in 9 days	No significant change

TABLE XIV. PENICILLIN IN DERMATOLOGIC INFECTIONS

AGE (YR.)	DIAGNOSIS	CULTURE	PENICILLIN TREATMENT	RESULTS
28	Sycosis vulgaris	Beta hem. Str.; hem. Staph. aureus	15,285,000 U. in 52 days + local	Failure, in spite of daily dosage up to 480,000 U. and later addition of local therapy
36	Sycosis vulgaris	Beta hem. Str.; hem. Staph. albus	14,560,000 U. in 60 days + local	14 days of 120,000 U. daily + local failed but infection finally yielded to 320,000 U. daily + local
23	Deep acne, severe, with infected cyst formation	Hem. Staph. albus; proteus	12,925,000 U. in 52 days	First 200,000 U. daily + local failed; surgery and penicillin succeeded
21	Deep acne, severe with infected cyst formation	Proteus, pyocyanus; hem. Staph. aureus and albus	16,720,000 U. in 52 days	First 200,000 U., then 360,000 U. daily failed; surgery and penicillin succeeded
50	Pustular dermatitis, bacterid type (Andrews)	Hem. Staph. aureus coagulose positive; diphtheroids	1,185,000 U. in 10 days	Cleared except for residual scaling; patient refused further treatment, superior to sulfonamide

eight months' duration, respectively. Both presented indurated lumpy lesions with active sinuses. One patient received a three-week course of 6,720,000 units intramuscularly, during which all traces of the disease other than the scars disappeared. Three months later there was no evidence of recurrence. The second patient received a six-week course of 14,945,000 units with apparent cure, only to develop a proved recurrence one month later. Thereupon a suprahyoid block dissection was performed while the patient was receiving 40,000 unit doses every three hours. The wound healed per primam and penicillin was continued for twenty-four days postoperatively.

The difference in response of these two patients to penicillin suggests wide variability in susceptibility among the actinomyces. The prompt recurrence in the second case after apparent cure suggests that the fungus, sealed within the dense scar tissue of the lesion, is not accessible to the drug. It suggests also that the involved tissue should be radically excised whenever possible.

*Suppurative parotitis:* One would expect that suppurative parotitis usually caused by one of the pyogenic cocci and characterized, at least in its early stage, by nonsuppurative cellulitis, would respond readily to penicillin. In our two patients, both of whom received 25,000 units intramuscularly every three hours, response was dramatic.

**CASE 1.**—An otherwise healthy young sergeant had early moderate left parotitis culturing hemolytic *Staph. aureus* susceptible to .01 units and alpha hemolytic *Str. salivarius* susceptible to .0012 units. Temperature and tenderness subsided in twenty-four hours and resolution was complete in ninety-six hours.

**CASE 2.**—A 59-year-old patient, hypertensive, with renal failure and severe azotemia (B.U.N. 97) developed over two days' time a large, very painful and exquisitely tender, hot swelling of the right gland. Complete relief of pain and definite reduction of swelling came within twelve hours and by the fifth day when therapy stopped, there remained only a small, nontender swelling. No drainage was noted, hence no culture was obtained.

*Ulcerative colitis:* Two patients with severe, chronic ulcerative colitis of 5 and 9 months' duration with typical roentgenologic findings and nonspecific stool cultures showed no improvement on penicillin therapy. One received 2,940,000 units over thirteen days, the other 6,806,000 units over twenty-eight days, as well as colonic irrigations of penicillin solution. The latter patient later showed improvement on sulfasuxidine.

*Gonorrhea in women:* Following the initial case, women with gonorrhea were turned over to Major Laman Gray, Chief of the Women's Surgery Section. An important observation was made by Gray in his twelve reported cases,<sup>26</sup> namely, that although the local and systemic infection was rapidly controlled, almost invariably the patient was left with bilateral tubo-ovarian masses and, therefore, with a prospect of probable sterility. In the case here presented the small tubo-ovarian abscesses might have been overlooked but for the gynecologist's specialized touch.

A 22-year-old woman with severe, early gonorrheal peritonitis, apparently the initial infection, was given 15,000 units penicillin intramuscularly every three hours for seven days. The vaginal smear and culture were negative within twelve hours. Within forty-

eight hours the initial temperature of 102.8° F. returned to normal and the patient felt greatly improved. On the seventh day of treatment the patient was practically well, clinically, and vaginal cultures remained negative, but bilateral tubo-ovarian masses were made out by the gynecologist. The sedimentation rate was 19. At final discharge sixteen days later the tubo-ovarian masses were little changed but the sedimentation rate had dropped to 6.

*Early syphilis:* Our single case is presented briefly.

A 16-year-old white married woman was admitted to Walter Reed General Hospital with severe hemorrhagic encephalitis complicating neoarsphenamine therapy for early secondary syphilis. Kahn and Wassermann tests were both 4 plus. On Nov. 24, 1943, 30,000 units of penicillin intramuscularly at three-hour intervals were started and a total of 4,645,000 units were injected over a twenty-nine-day period. The serologic titers progressively weakened until by Feb. 9, 1944, both Kahn and Wassermann were negative. From recent careful work by Moore and associates<sup>27</sup> a much smaller dosage has been found effective in these cases.

*Nephritis:* Three patients with acute exacerbations of chronic glomerulonephritis received 25,000 units of penicillin every three hours for fourteen days, or a total dose per patient of 2,800,000 units. No significant alteration of the sedimentation rate, Addis count, urine albumin content, or renal function studies was noted during therapy or for the three months thereafter that the patients were under observation.

*Rheumatic fever:* Three patients with acute rheumatic fever were treated with intramuscular injections of penicillin for fourteen days, two patients receiving 25,000 units every three hours, the third receiving 45,000 units at similar intervals. There was no appreciable clinical improvement or change in the sedimentation rate. Others<sup>28, 29</sup> in more extensive studies have reached similar conclusions.

*Tuberculosis:* Although it is established<sup>30, 31</sup> that penicillin exerts no in vitro or in vivo effect upon the tubercle bacillus, it was thought advisable by some to make a clinical trial in two cases. Needless to say, neither patient showed any response to the drug. The first, with tuberculous meningitis, received 10,000 to 20,000 units intrathecally and 480,000 units intramuscularly each day for five days. The second patient with tuberculous pneumonia and pleural effusion, first suspected of coccidioidomycosis, received 3,220,000 units over a ten-day period.

*Chronic brucellosis:* Penicillin was administered over an eight- to ten-day period to two patients with chronic brucellosis. Blood cultures were sterile in both patients. Agglutination tests for *B. abortus* and *B. melitensis*, brucellergin skin tests, and opsonocytophagic indices were not significantly altered during or after treatment nor was there any clinical improvement in either case. One patient, an 11-year-old boy with periodic bouts of fever, received a total of 760,000 units in eight days. The second patient, who had secondary uveitis, was given 3,600,000 units over a ten-day period. Longer periods of therapy and larger doses are indicated before a final appraisal of the efficacy of penicillin can be made. Both *B. melitensis* and *B. abortus* have been found to be susceptible to penicillin in vitro.<sup>30, 32</sup>



*Iridocyclitis:* Our experience is limited to two cases.

(1) Uveitis secondary to focalized chronic brucellosis (noted previously) failed to improve after ten days of 45,000 units intramuscularly at three-hour intervals.

(2) Iridocyclitis, bilateral, slowly progressive, cause unknown, made no improvement after twenty-one days of intensive treatment totalling 4,955,000 units.

#### SUMMARY

1. A review is presented of the laboratory and clinical experience of the Walter Reed General Hospital penicillin committee from July, 1943, through September, 1944.

2. The analysis includes 255 conditions in 220 patients for which penicillin treatment was administered.

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# A SAFETY FACTOR IN GASTRIC RESECTION

## PRELIMINARY REPORT

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**A** LIMITED but encouraging experience warrants this brief preliminary report upon a new device designed to reduce materially, if not to eliminate entirely, one of the most dangerous hazards of gastric resection—disruption of the duodenal stump.

Disruption of the duodenal stump following gastric resection and anastomosis by any one of the Billroth II modifications occurs often enough to make it a prominent feature in the surgical literature dealing with the treatment of gastric ulceration or malignancy. It is not our purpose to present a résumé of the literature in this initial report but rather to emphasize the danger of this complication, the very high mortality associated with it, and to stress a means for its prevention.

In my opinion, by far the most common cause of stump leakage is increased pressure within the duodenal lumen consequent upon obstruction, partial or complete, at the anastomotic site. In the best of hands, angulations and kinks at the stoma do occur. Individual variations and conditions found at operation require variations in technique. Hypoproteinemia with its consequent edema may play a part in closing a lumen otherwise competent. But from whatever cause arising, an obstruction of the proximal duodenum leaves no egress for the bile, pancreatic secretions, and the secretions of the duodenum itself, amounting to approximately 1,500 c.c. in twenty-four hours. This increased intraluminal pressure then seeks an alternative outlet which results in bringing too much stress to bear upon a stump however carefully it may have been sutured.

The T tube here reported and illustrated was designed primarily for usage in the Hofmeister-Polya type of anastomosis as elaborated and popularized by the Lahey Clinic. However, other models are available adapted for use in the Polya anastomosis where the entire cut end of the stomach is employed for union with the jejunum.

The tube is more easily illustrated than described, and a reference to Figs. 1 to 3 is all that is required. It is smooth of surface, presenting one vertical portion of the inverted T, which fits loosely into the gastric part of the stoma, and the other, the long curved horizontal portion, resting in the jejunum, one end of which extends well proximal and the other end of which extends well distal to the anastomotic site. At no point does the tube exert any pressure upon the bowel wall. It is inserted into the anastomosis after all but the suturing of the anterior wall of the stomach and jejunum has been completed. The tube is fastened into the stoma by a figure-of-eight suture passing through the posterior wall of the anastomosis and tied around the tube. This suture may be

of silk or gastrointestinal chromic as desired. The anastomosis is then completed in the usual fashion.

Reference to the illustrations will show at once the obvious merits of this device. The multiple fenestrations encourage free flow of duodenal and gastric secretions into the distal jejunum and make it impossible for blocking to occur. The presence of the tube during the final stages of the anastomosis serves as a mold over which more accurate suturing can be performed and as a safeguard against kinks and angulations. Should postoperative edema occur, the tube prevents obstruction from this cause.

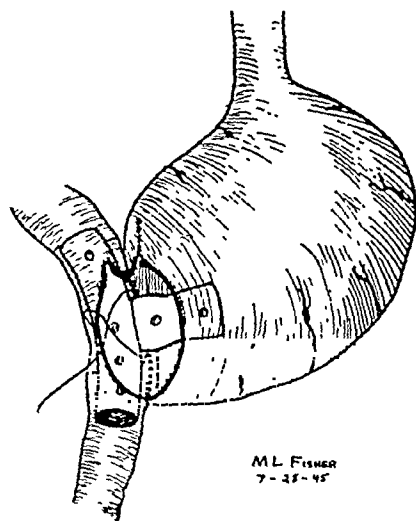
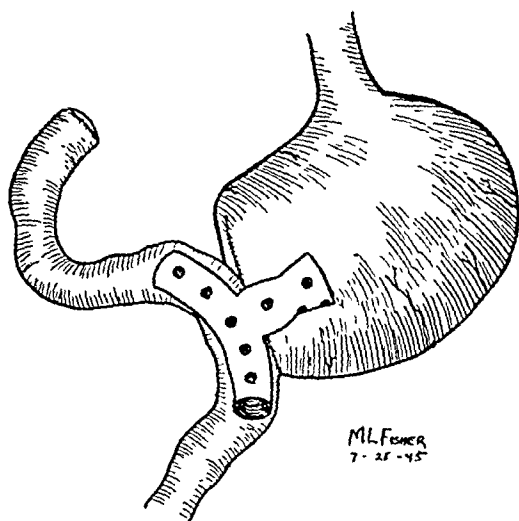


Fig. 1.—Diagrammatic representation of the T tube in position.

Fig. 2.—Diagrammatic representation of the T tube being placed loosely in the gastro-jejunal stoma.

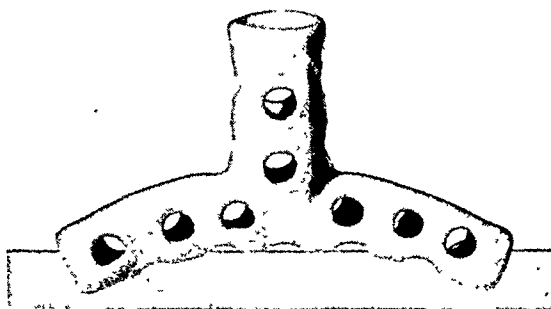


Fig. 3.—Photograph of the T tube.

As noted by Mr. Miller in a later portion of this article, the tube disintegrates within a period of about ninety-six hours, thus furnishing a dependable framework for the anastomotic stoma during that period when obstruction may occur, but dissolving and removing that framework when it is no longer required. Mr. Miller's extensive experience with this product enables him to time this disintegration quite accurately.

The use of this tube would in no manner preclude the use of the Abbott-Rawson tube at the same time. It is, however, my opinion that the T tube will obviate this necessity and will permit the discharge of liquids from the stomach into the distal jejunum very early postoperatively. Further experience is necessary to determine that point.

The following description of the chemistry and mechanics involved is furnished by Mr. Grover C. Miller, chemist of the Seal-Ins Laboratories, whose pioneer work on enteric coatings for tablets and capsules is well known.

"The Alesen T tube is a further development of the principle used in the timed enteric coating for tablets and capsules discovered by Grover C. Miller several years ago. The dependability of this coating has been proved by the following investigators: Worton, Kempf, Burrin, and Bibbins,<sup>1</sup> Wright and Brady,<sup>2</sup> Faust,<sup>3, 5</sup> and Miller and Choquette.<sup>4</sup>

"The material used in making these tubes\* varies somewhat from the enteric coating, but the principle is the same. Percentages are changed to meet the timing requirements. These tubes are composed of the following: stearic acid, U.S.P., carnauba wax No. 1, white purified beeswax, petroleum jelly, powdered elm bark, and an antiseptic, merthiolate 1 to 7000. Also barium sulfate is combined in the mixture so it is possible to x-ray the patient at any time during the disintegration of the tube. This material has a melting point of approximately 85° C. The purpose of the powdered elm bark is to absorb water and expand: the expanding gradually splits away the waxes and permits a further penetration of the moisture into the wall. The timing is controlled by the percentage of elm bark used.

"The Alesen T tube is timed to disintegrate in approximately ninety-six hours. The tube may be sterilized by placing it in a zephiran chloride solution, 1 to 1000, for fifteen minutes at room temperature.

#### HOW MADE

"The tubes are molded in 55, 60, and 65 mm. lengths on a 6 mm. rod curved to 115 mm. circle. The gastric tip of the T is molded on a 11 mm. rod. The gauge of the wall is of approximately 2 mm. thickness."

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\*The T tubes may be obtained from the Seal-Ins Laboratories, Los Angeles, Calif.

## HYPERURICEMIA IN GASTRIC CANCER

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THE value and significance of an adequate protein balance to the surgical patient have been studied by many authors on innumerable occasions. In previous studies that I did with Adams<sup>1, 2</sup> we were able to differentiate hypoproteinemia secondary to insufficient dietary protein from hypoproteinemia secondary to accelerated endogenous protein depletion. This differentiation was made possible by an evaluation of blood uric acid.

Blood uric acid will rise in the presence of endogenous hypoproteinemia. This results from the patient's attempts to replenish his protein deficiency through endogenous protein secured from his own body. Clinically this state is revealed in the loss of strength and weight. Chemically it can be demonstrated in an elevation of uric acid. The greater the hyperuricemia the more accelerated is the rate of endogenous protein metabolism. The reason for the hyperuricemia is the fact that uric acid is one of the end products of endogenous protein metabolism.<sup>2</sup>

When uric acid is the end product of body purine metabolism it is called endogenous uric acid. The term endogenous is used to distinguish the uric acid formed from the purines produced in the course of the digestion of food proteins. Endogenous uric acid is derived from the breakdown of nuclear material found in muscle tissue and glandular structures. An increase in endogenous uric acid results in an elevation of blood uric acid (normal value taken is 3 mg. per 100 c.c. of serum). A uric acid value above this level is termed hyperuricemia.

In considering hyperuricemia, other causes for an elevated blood uric acid must be remembered. Primary liver disease may produce hyperuricemia if the disease process is sufficiently advanced to result in impaired hepatic physiology. Since uric acid destruction occurs in the liver a resulting hyperuricemia is easily understood. Renal failure also causes an early rise in blood uric acid. The status of the liver and kidneys can be determined by specific chemical tests directed at evaluating these organs. When the liver and kidneys are not primarily impaired, a pre-existing hypoproteinemia accelerates endogenous purine metabolism. This accelerated endogenous metabolism results in hyperuricemia. The significance of hyperuricemia is that it is an indicator of the degree of endogenous protein metabolic activity. Thus a graphic picture of the patient's nutritional state can be evaluated by a physiochemical analysis of the blood.<sup>2</sup>

In order to interpret adequately the relationship between serum protein and serum uric acid, both determinations must be performed simultaneously. It has been found that patients with gastric cancer usually have a lowered serum protein. This hypoproteinemia results because of a loss of appetite, especially for meat, and the fear of eating because of nausea and vomiting.

TABLE I. PROTEIN AND URIC ACID VALUES IN GASTRIC CANCER PATIENTS WITH SLIGHT HYPERURICEMIA

CASE	AGE (YR.) SEX	SERUM PROTEIN	SERUM URIC ACID	WEIGHT LOSS (LB.)	PERIOD OF WEIGHT LOSS (MO.)
1	42 M	6.2	3.9	12	6
2	49 M	6.5	3.7	10	8
3	57 M	6.1	3.9	12	7
4	60 F	6.0	4.0	15	6
5	50 M	6.5	3.7	10	8
6	49 M	6.0	4.0	14	7
7	63 F	6.0	3.9	13	6
8	57 M	6.1	3.9	14	6

TABLE II. PROTEIN AND URIC ACID VALUES IN GASTRIC CANCER PATIENTS WITH MODERATE HYPERURICEMIA

CASE	AGE (YR.) SEX	SERUM PROTEIN	SERUM URIC ACID	WEIGHT LOSS (LB.)	PERIOD OF WEIGHT LOSS (MO.)
1	52 M	5.5	4.2	15	6
2	63 F	5.5	5.0	23	4
3	55 M	5.9	5.0	25	4
4	57 M	6.0	4.5	16	6
5	55 M	5.5	4.9	20	5
6	58 F	6.0	4.5	15	6

TABLE III. PROTEIN AND URIC ACID VALUES IN GASTRIC CANCER PATIENTS WITH MARKED HYPERURICEMIA INCLUDING POSTOPERATIVE COMPLICATIONS

CASE	AGE (YR.) SEX	SERUM PROTEIN	SERUM URIC ACID	WEIGHT LOSS (LB.)	PERIOD OF WEIGHT LOSS (MO.)	POSTOPERATIVE COMPLICATION
1*	56 M	5.0	5.0	25	4	Gouty arthritis
2	62 M	4.5	5.2	30	3	Bronchopneumonia and wound infection
3*	57 M	4.5	5.5	30	2	Gouty arthritis
4	62 M	4.5	5.4	25	4	Bronchopneumonia
5	67 M	5.0	5.0	25	4	Wound dehiscence
6	65 F	4.5	5.2	25	3	Bronchopneumonia and wound infection

\*Cases previously reported elsewhere.<sup>1</sup>

The diet usually consists of simple fluids without adequate protein. The result is an inevitable progressive hypoproteinemia. Hypoproteinemia of this type usually is associated with a hyperuricemia. The lower the protein level, the higher will be the uric acid level.

A normal uric acid in the presence of a hypoproteinemia signifies that a sufficient amount of exogenous protein is available to prevent the utilization of endogenous protein. This indicates that sufficient protein is available to satisfy the basic protein requirements of the surgical patient with gastric cancer. An intelligent interpretation of blood uric acid in association with serum protein values will indicate the ratio between exogenous and endogenous protein metabolism. These studies have been employed in twenty patients with gastric cancer. From these studies a physiochemical prognostic guide to the nutritional state of the patient with gastric cancer was available. Current observations, discussion, and conclusions on hyperuricemia in gastric cancer follow. (See Tables I, II, and III.)

## DISCUSSION

The majority of patients with gastric cancer have an alteration in their normal dietary regime. As the disease progresses complete loss of appetite may occur followed by an almost total abstinence of food because of nausea and vomiting. This results in an inadequate protein intake and a subsequent hypoproteinemia. The daily protein requirement can be determined from the amount of nitrogen eliminated in the feces and urine in twenty-four hours. This total nitrogen excretion per day multiplied by 6.25 will give the approximate amount of protein destroyed over twenty-four hours in the gastric cancer patient. An intake of protein equivalent to the protein destroyed in the body will usually suffice to keep the human body in positive nitrogen balance. This basic protein requirement for an average man (70 kg.) is 70 Gm. The present studies concern the gastric cancer patient who does not obtain this basic requirement of 70 Gm. of protein.

As has been previously stated, the lack of protein intake quickly results in a hypoproteinemia. The human body attempts to correct this disturbed physiologic state by calling upon the body protein. This stimulus accelerates endogenous protein metabolism with a subsequent increase in blood uric acid.

Current observations on this topic have led to the belief that a causal relationship exists between hyperuricemia and hypoproteinemia. This belief is founded upon many more studies of uric acid and protein than are presented here. An indication of the relationship between the two may be gleaned from Fig. 1.

Specific study of twenty patients with gastric cancer has corroborated the interrelationship between hyperuricemia and hypoproteinemia. We have divided these cases into three groups according to the degree of hyperuricemia. The terms mild, moderate, and marked are employed to identify each group.

The first group of eight patients had slight alteration in serum uric acid and the patients categorized as having mild hyperuricemia. The uric acid values ranged from 3.7 to 4 mg. per 100 c.c. of serum. Serum protein determinations were 6 to 6.3 Gm. per cent. This uric acid value is taken as the uppermost limit of normal, and the protein as the lowest normal level. Patients in this group appeared to have secured a harmonious balance between exogenous and endogenous protein metabolism. These patients had a diminished protein intake but no complete lack of exogenous protein. In this group weight loss was the least (ten to fifteen pounds) and extended over a period of from six to eight months. These patients had the best prognosis, the least postoperative complications, and were restored to positive nitrogen balance rapidly.

In the intermediate group, the six patients were categorized as having moderate hyperuricemia. The uric acid values in this group ranged from 4 to 5 mg. per cent with protein values of 5 to 6 Gm. Patients falling into this category gave a history of fifteen to twenty-five pounds loss of weight over a period of four to six months. In general these patients tolerated operation well after an adequate preoperative regime which included a correction



of the hypoproteinemia. Postoperative complications were infrequent and when present were of minor consideration.

Particular interest here concerns the last group of six patients who had pronounced hyperuricemia. These patients had insufficient protein intake which produced a hypoproteinemia. In order to compensate for this lowered protein level, protein was mobilized from the body tissues to rectify the hypoproteinemia. The serum uric acid level became elevated since it is an end product of endogenous protein metabolism. This accelerated endogenous

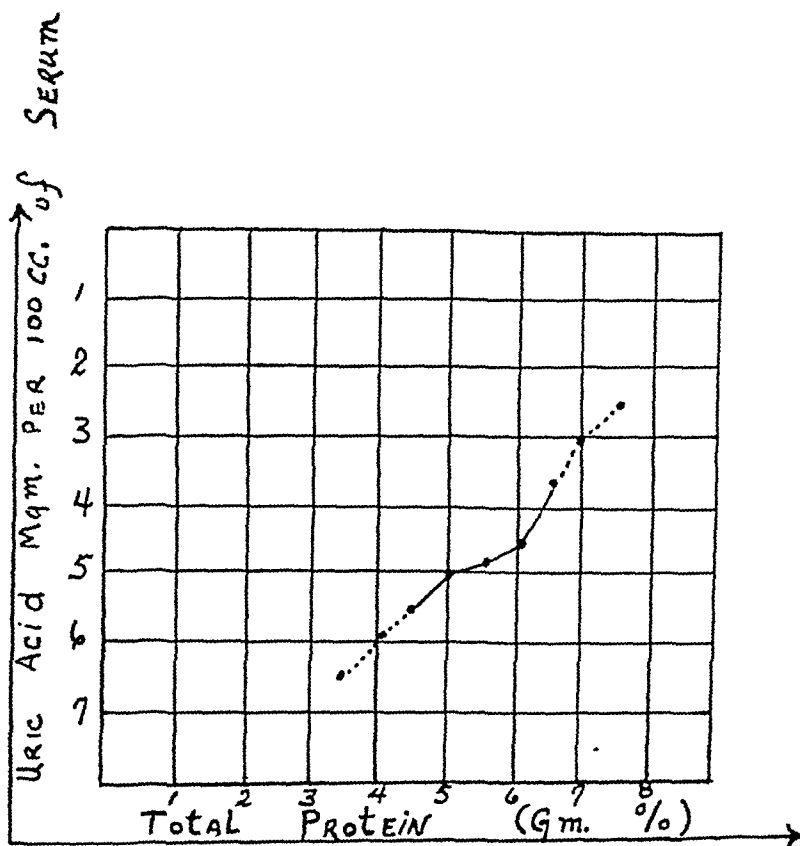


Fig. 1.—Graphic relationship between hyperuricemia and hypoproteinemia. Completed line indicates the relationship between total protein and uric acid values based upon cases presented. Incompleted lines suggest further ratio as revealed in other case studies.

protein metabolism was displayed clinically by a loss of twenty-five to thirty pounds over a period of two to four months. Accelerated endogenous protein metabolism of this type is characterized by a rapid loss of weight over a short period of time. Physiochemically it is demonstrated by a low protein and a high uric acid. In the six patients studied the serum protein fell to a level of 4 to 5 Gm.; the serum uric acid value rose to 5 and 5.5 mg. per cent.

Hyperuricemia as displayed by this group is significantly valuable as a prognostic guide to postoperative complications. Studies of many cases falling into this category, in addition to those discussed here, have indicated that most complications occur in patients with marked hyperuricemia. These

complications may be slight or severe. The most frequently encountered complications are:

1. Muscle weakness and fatigability
2. Nutritional edema
  - (a) Edema of sacrum and ankles
  - (b) Edema of anastomosis, stoma, and gastrointestinal mucosa
  - (c) Delayed wound healing and/or wound dehiscence
  - (d) Circulatory insufficiency
    - (1) Diminished urinary output
3. Lowered resistance to infection
  - (a) Wound infection
  - (b) Postoperative pneumonitis
  - (c) Urinary infections
4. Postoperative gouty arthritis

Of all the postoperative complications mentioned the most interesting is postoperative gouty arthritis. A definite pattern in the production of postoperative gouty arthritis cannot be stated without dispute. However, in a previous publication a pathway in the production of this complication was postulated.<sup>1</sup> The mechanism advanced was that in the presence of a hypoproteinemia, endogenous purine metabolism is accelerated. This accelerated metabolism results in a hyperuricemia which is the precipitating agent for the deposition of urate crystals on a previously damaged cartilaginous joint surface. In my report with Adams<sup>1</sup> of five instances of postoperative gouty arthritis, all patients had a varying degree of osteoarthritis. From this it can be appreciated that hyperuricemia may have a more far-reaching significance than is apparent at the present time.

Apropos of this statement, recent experimental publications on the effects of a low lysine diet on the growth of spontaneous mammary cancer may find some association with uric acid metabolism.<sup>3</sup> Briefly, this research has shown that the rate of tumor growth in mice can be inhibited for short periods of time when a diet is administered in which lysine is deficient. (Lysine, an essential amino acid, has been established as essentially a growth factor.) This is further substantiated by the rapid rate of tumor growth when lysine is added to the diet. On the basis of these observations it seems that neoplastic tissue, like normal somatic tissue, requires protein for growth.<sup>3</sup> It seems logical that this needed protein is taken from the protein reserves of the body. This was proved by the fact that the experimental animals had a marked weight loss.<sup>3</sup> Apparently this situation paralleled the loss of weight observed in the patients previously presented.

In view of this experimental observation on mice, another factor in the acceleration of endogenous protein metabolism appears to be at work producing a hypoproteinemia. This hypoproteinemia may be increased because a growing cancer will utilize the most readily available body protein. This new source of increased endogenous protein metabolism, in addition to other factors previously mentioned, will further increase the hyperuricemic state. Perhaps

additional future studies on hyperuricemia may bring to light some method of calculating the rate and extent of cancer growth.

#### SUMMARY

1. Attention is called to the significance of hyperuricemia in the exact evaluation of the nutritional state of patients with gastric cancer.

2. The importance of serum uric acid study in conjunction with serum protein determinations is stressed.

3. Twenty gastric cancer patients with alterations in serum uric acid and protein were studied and the results presented.

4. According to the degree of uric acid elevation, these patients have been categorized as having mild, moderate, or marked hyperuricemia.

5. Each group is discussed in terms of weight loss and the length of time over which the loss occurred. Emphasis is placed on those patients with marked hyperuricemia.

6. Many of the complications associated with hypoproteinemia and hyperuricemia, including postoperative gouty arthritis, were found in the group with marked hyperuricemia.

7. Mention is made of recent cancer research on the growth of cancer and the possible association of the rate of cancer growth with the facts presented here.

#### CONCLUSIONS

The present physiochemical analysis of twenty patients with gastric cancer coincides with the current study on the relationship between hypoproteinemia and hyperuricemia. This interrelationship indicates that a more complete evaluation of the nutritional state of the surgical patient can be obtained by studying the blood serum uric acid in conjunction with a serum protein determination. Heretofore it was believed that protein study alone was sufficient in evaluating the nutritional state of the body. It is hoped that the significance of hyperuricemia in patients with gastric cancer has been emphasized. The importance of hyperuricemia is stressed, first, because it differentiates hypoproteinemia subsequent to insufficient exogenous protein from hypoproteinemia resulting from accelerated endogenous protein metabolism. Thus, the exact source of protein depletion can be identified and corrected. Second, it will assist in foretelling postoperative complications usually associated with a debilitated nutritional state in patients with gastrointestinal cancer.

Many of the cases reported in this study were investigated by the author during his Fellowship in Surgery at the Lahey Clinic, Boston, Mass.

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## MULTIPLE CARCINOMAS OF THE STOMACH

### CASE PRESENTATION WITH FIVE PRIMARY SEPARATE MALIGNANT LESIONS TREATED BY TOTAL TRANSTHORACIC GASTRECTOMY

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THERE has been a great deal of progress made in the technique and end results in transthoracic resections of the stomach since the first successful ones were done by Ochsner and DeBakey in 1938.<sup>1-3</sup> Although the abdominal route to total gastrectomy in most hands still offers less risk to the patient,<sup>4-6</sup> there are many lesions involving the lower end of the esophagus which cannot be attacked by this approach. The first successful total gastrectomy by the transthoracic route was done by Willy Meyer in 1942.<sup>7</sup> Since that time Sweet has reported eighteen cases with seven deaths, a mortality rate of 38.8 per cent, which results compare favorably to those resections done by the abdominal route.<sup>8-11</sup> The success of surgery of this magnitude in these debilitated patients depends on adequate preoperative preparation; rapid, careful surgical technique with expertly administered anesthesia; and careful postoperative care.

The occurrence of multiple benign lesions of the stomach has been reported several times, and, although multiple malignancies of the gastrointestinal tract are second most frequent to skin lesions,<sup>12</sup> multiple malignancies of the stomach are comparatively rare lesions. Walters, Gray, and Priestly<sup>13</sup> stated that malignant growths of the stomach are invariably single, but pointed out that frequently there is little to distinguish a malignant from a benign growth microscopically. Brindley, Dockerty, and Gray<sup>14</sup> reported twenty-three multiple malignancies of the stomach out of 1,184 carcinomas of the stomach seen at the Mayo Clinic between 1932 and 1941, an incidence of 1.94 per cent; and they reported an additional patient with four adenocarcinomas of the stomach. Owen<sup>15</sup> in 1921 reported a patient with four primary malignancies of the stomach. Of all patients with multiple primary malignancies at autopsy, multiple malignant lesions of the stomach occupy about 2.8 per cent.<sup>12</sup>

The case to be presented is doubly interesting in that the patient had five primary cancerous lesions of the stomach and he was treated by transthoracic gastrectomy.

#### CASE REPORT

H. G. (I 44 152199).—A 54-year-old Negro man entered Charity Hospital Sept. 19, 1944, complaining of pain in the epigastrium of four months' duration. The pain started while the patient was receiving anti-syphilitic therapy from his local physician. Once the pain started it remained as a constant burning pain which was not relieved by soda or food.

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He vomited at least once daily but not at any particular time of the day. During the four-month period his weight decreased from 125 to 103 pounds, a loss of twenty-two pounds. The past history was essentially negative. No primary syphilitic history was obtained.

*Physical Examination on Admission.*—The patient, of above average intellect, had no acute distress. Blood pressure was 84/7; temperature, 100.4° F.; pulse, 74; respirations, 20. The skin showed evidence of chronic dehydration. Head and neck were found essentially negative. In the chest, the lungs and heart were essentially normal. The abdomen was soft, with no masses, and slight guarding in the epigastrium. There were no scars.

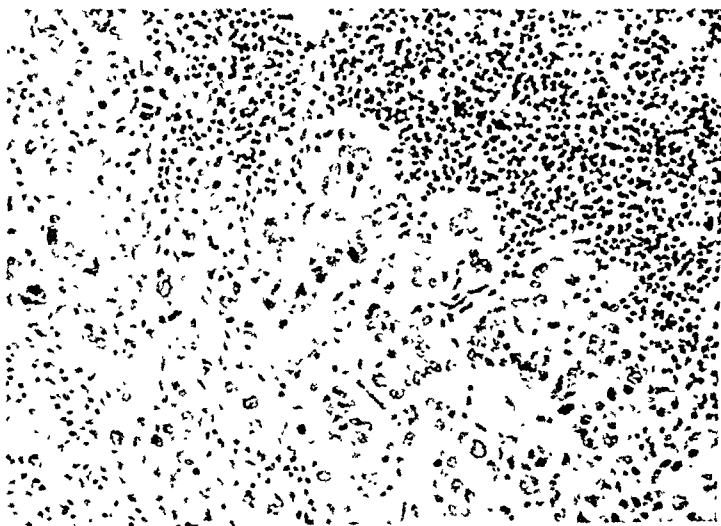


Fig. 1.—Lymph node from lesser curvature showing infiltration by adenocarcinoma ( $\times 200$ ).



Fig. 2.—The first tumor, at the cardia, showing diffuse infiltration of the wall of the stomach by the neoplastic tissue ( $\times 61$ ).

Genitals were normal. Rectal examination revealed no masses and no rectal shelf. Extremities and reflexes were normal.

The admitting diagnosis was carcinoma of the stomach.

*Laboratory.*—September 20, hemoglobin was 12 Gm.; white blood cells, 5,200; normal differential. Urine was essentially negative.

September 22, gastrointestinal series showed no abnormalities of the esophagus or duodenum. A small ulcer was found on the prepyloric portion of the stomach.

October 2, blood urea nitrogen was 8.7. Hippuric acid liver function test was normal.

The diagnosis remained carcinoma of the stomach despite the x-ray report.



Fig. 3.—The second tumor in the body, showing junction of normal and malignant tissue; note tortuous malignant glands ( $\times 200$ ).

Oct. 5, 1944, exploration was done through an upper midline incision. A large carcinoma of the cardia was found which had extended into the thoracic esophagus. A smaller very soft lesion was palpable at the pylorus which did not seem to involve the muscularis or the serosa over it. There were several small lymph nodes in the lesser omentum, but there were no palpable nodules in the liver. The greater omentum contained several small nodes at the pylorus but these were soft. The rest of the abdomen was thoroughly explored and was essentially normal. The stomach was then opened; the small soft lesion at the pylorus was biopsied and the stomach was then closed. The lymph nodes at the pylorus were removed and together with the biopsy of the lesion at the pylorus were sent for frozen section. The gastric lesion was reported as malignant and nodes showed no evidence of malignancy. It was obvious that any curative procedure would have to be done by the transthoracic route because of the extent of the lesion at the cardia. The stomach was then thoroughly mobilized by removing the greater omentum from the transverse colon and the lesser omentum from the liver. The left gastric, left gastroepiploic, and right gastroepiploic vessels were then ligated and divided near their origins, and the greater and lesser omenta were sutured to the anterior surface of the stomach. The abdomen was then closed using chromic catgut No. 000 for the peritoneum, and interrupted cotton sutures for the fascia and for the skin. The patient was given 500 c.c. whole blood on the operating table. Convalescence was excellent and the patient was given a high protein, 4,000 calorie diet on the first postoperative day. Sutures were out on the ninth day. He was scheduled for the second stage of the operation on Oct. 20, 1944, but this had to be canceled because of an upper respiratory infection.

On Oct. 27, 1944, through a ninth intercostal space incision a total transthoracic gastrectomy was performed. Considerable difficulty was encountered separating the stomach from the pancreas but otherwise no special difficulties were experienced. About two and one-half inches of esophagus and the stomach were removed with the stomach. An anastomosis was made between the jejunum and the esophagus in the chest cavity, using an inner row of continuous lock chromic catgut No. 000 and an outer row of interrupted quilting cotton. The Levin tube was threaded into the distal jejunal loop for feeding. The patient was given 2,500 c.c. of blood on the day of operation. The postoperative course was excellent. Tube feeding was started on the first postoperative day through the Levin tube that had been



Fig. 4—The third tumor in the body, showing junction of normal and malignant glandular tissue note loss of differentiation in the malignant cells in the upper half of the section in contrast to the well-differentiated glandular cells below ( $\times 200$ ).



Fig. 5—The fourth tumor in the body, note malignant cells infiltrating the submucosa and the malignant cells in this group smaller and more anaplastic than those of the other tumors in the body ( $\times 200$ ).

placed in the distal jejunal loop. Oral feeding of a high caloric soft diet was started on the third postoperative day because the patient pulled out the jejunal tube. Nov. 3, 1944, he was given 500 c.c. of whole blood to correct the anemia. A wound infection was drained on November 7, and opened into the chest cavity on November 9. This wound continued



Fig. 6.—The fifth tumor, in the pylorus, note the malignant thrombus on the left side ( $\times 61$ ).



Fig. 7.—A different magnification of the second tumor, showing large tortuous malignant glands ( $\times 61$ ).



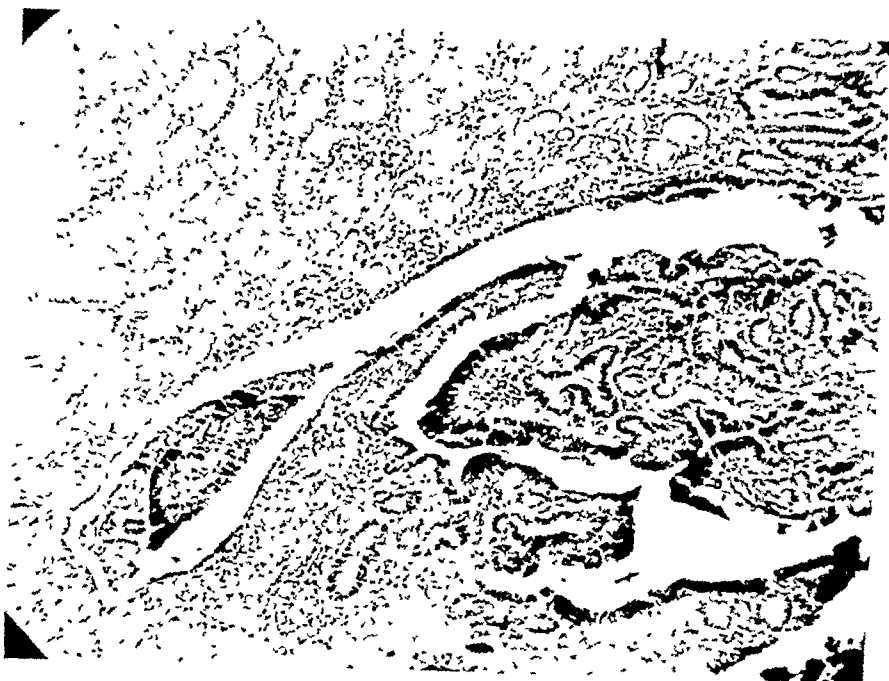


Fig. 8—A different magnification of the fourth tumor in the body, showing junction of benign and malignant tissue with malignant infiltration of the submucosa ( $\times 61$ ).

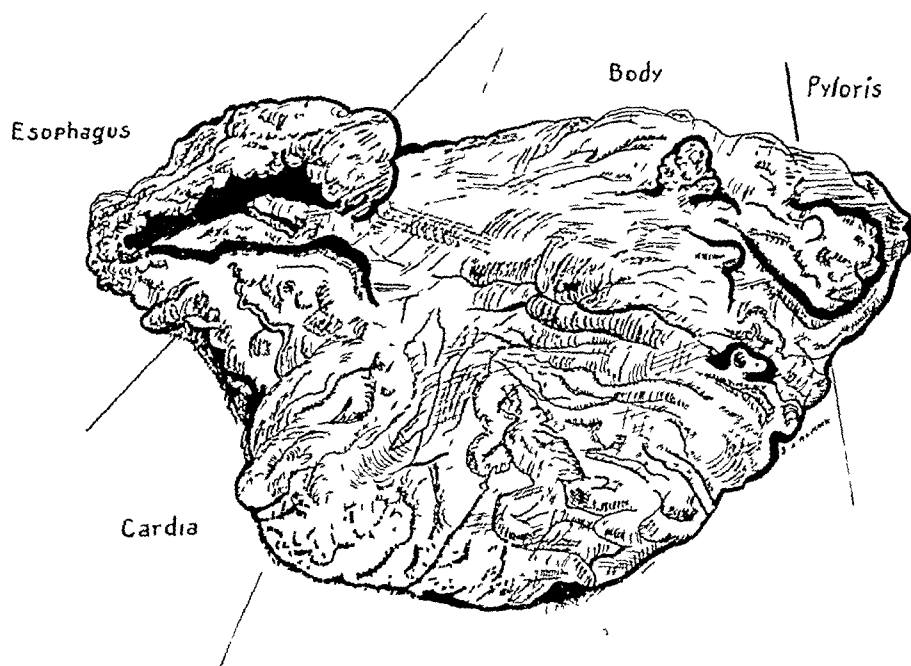


Fig. 9—The stomach is opened along the posterior surface near to the lesser curvature. The normal esophageal mucous membrane is folded back and does not show well. The large tumor of the cardia can be seen extending into the esophagus. The deep ulceration in this tumor lies mainly in the esophagus. This tumor had metastasized to the lymph nodes of the lesser omentum, it involved all of the layers of the stomach wall. Three small pedunculated growths are present in the body. These were limited by the submucosa and did not invade the muscle. Although much alike microscopically, these tumors were separated by normal mucosa and submucosa. The papillomatous growth at the pylorus is 3 cm in diameter at the base but also does not involve the muscularis. This is the tumor that was biopsied at the first operation.

to drain until December 6, at which time a large silk suture which had been used to approximate the ribs was extruded, after which the wound rapidly healed. Gastrointestinal series on November 28 showed no fistula and a large dilated upper jejunum which emptied rapidly. The patient was discharged on December 11 in good condition.

He took care of his farm until February 14, at which time distention began. His local physician cared for him at home until his death, Feb. 28, 1945, which was attributed to carcinoma of the rectum. No biopsy was taken and autopsy was not available. He did not return to the hospital after being discharged and the only follow-up was obtained through the local social service worker. It seems more logical to suspect that death was due to metastases from the large carcinoma of the cardia, rather than a new carcinoma of the rectum, as his rectum was negative to digital examination at this hospital.

*Pathology Report.*—The specimen consisted of 6 centimeters of esophagus, the entire stomach including the pylorus, the greater and lesser omenta, and lymph nodes. The stomach had been previously opened and measured open 15 by 18 cm. A portion of greater omentum measuring 10 by 6 cm. with a thickness of 1 cm. was attached to the greater curvature. It consisted of numerous lobules of fat in which no firm nodules could be felt. The serosa of the stomach was pale yellow, smooth, and showed a few petechiae. Toward the cardiac end the wall of the stomach was very firm, rigid, and hemorrhagic. It measured in its thickest portion 3.5 cm. and extended 4.5 cm. from the resected border. The lumen of the cardia measured 2 cm. in its narrowest portion. The mucosal surface of the cardia was very coarsely granular, yellowish red with an ulcer in the central portion measuring 1 by .05 cm. and approximately 0.3 cm. in depth. The base of the ulcer was yellow and soft. The edges were smooth yellowish red, firm and rounded. The fundus of the stomach was soft and covered with a hemorrhagic mucus. Extending from the lesser curvature to the greater curvature were four sessile, pedunculated masses. The largest was 3 cm. in diameter at the base. They involved the mucosa and the submucosa, but not the muscularis. They were pale yellow, smooth with a few small furrows but not ulcerated.

*Microscopic Diagnosis.*—(1) Four papillary adenocarcinomas of the mucosa of the stomach apparently arising from adenomatous polypi. (2) Ulcerating carcinoma of the cardiac end of the stomach infiltrating the muscularis, with metastases to the perigastric lymph nodes.

#### SUMMARY

A case is reported with five primary carcinomas of the stomach treated by transthoracic total gastrectomy. As far as I could determine this is the first reported case of this type. A radical total gastrectomy was successfully performed transthoracically, but the patient died suddenly three months later after a sudden onset of distention, which may have been due to metastases.

My thanks to Dr. Charles Dunlap of the Department of Pathology of Tulane University and Mr. William Stewart of the photographic department of the Louisiana State Medical School for their help and advice in preparing the photographs.

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## EARLY DIAGNOSIS AND MANAGEMENT OF SMALL INTESTINAL OBSTRUCTION

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THE purpose of this discussion upon the early diagnosis and treatment of small intestinal obstruction is to emphasize the possibility of this condition in abdominal colic not localized to any quadrant or specific viscus in the abdomen.

Small bowel obstructions may be divided into those external, on the surface of the abdomen, and those hidden within the abdominal cavity.

Those on the surface of the abdomen are strangulated obstructions and are easily diagnosed. Rarely is there prolonged delay because the patient is aware that the long-existing hernia is no longer a symptomless affair but has suddenly become an irreducible mass, firm and hard. The abdominal pain and symptoms are associated with this persistent protrusion. The physician, more accustomed to recognize the significance of this clinical entity, promptly calls surgical consultation and operative intervention is instituted, usually before bowel gangrene intervenes.

We have not been sympathetic with attempted medical reduction of strangulated hernia. We know that, if successful, nothing permanent has been done to prevent its recurrence and that the viability of the reduced bowel is speculative. We know that it is better to reduce the bowel under direct vision, inspect it carefully for adequate circulation, and repair the hernial defect. Then, and only then, can one be certain of the viable continuity of the bowel and only then has anything been done to prevent a recurrence of the catastrophe. We, therefore, do not attempt manipulative reduction in strangulated hernia but advise immediate surgical repair.

Those obstructions within the abdomen are hidden from sight and the diagnosis is often delayed because the symptom complex is not appreciated by the attending physician. Delay in receiving medical attention is due to a belief by the patient that the abdominal pain is due to some insignificant cause. Often many harmful home remedies have been used. As the result of this delay and ill-advised treatment, serious complications often have developed. The situation is, therefore, frequently the result of delay of both patient and physician; consequently, when first seen the patient is in an advanced stage of small bowel obstruction, presenting distention, vomiting, and often peritonitis from bowel rupture.

The intra-abdominal small bowel obstruction may be a simple form of obstruction in which the viability of the bowel is not in jeopardy, or it may be a strangulated or volvulus type in which the blood supply is obstructed and

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gangrene is imminent. In the former, delay is not so serious and can be tolerated; in the latter, delay is serious and may mean the life or death of the patient.

The simple or nonstrangulated types of obstruction may result from bands of adhesion, angulation of the bowel by adhesive bands, or intrinsic lesions within the bowel, such as an obstructive gallstone or neoplasm. Immediate operation is not a problem in simple nonstrangulating obstruction. However, when the blood supply is damaged to a segment of small bowel, as happens in a strangulation, volvulus, or intussusception, it becomes of paramount importance and must be released at once, regardless of the physiologic resources of the patient, otherwise gangrene, rupture, and peritonitis will ensue. Here rehabilitation measures must, for the moment, be deferred in the interest of bowel viability. Thus the surgeon is faced with two problems in small bowel obstruction: First, a clear distinction must be made as to the probable nature of the obstruction. Second, the integrity of the blood supply to the bowel must be carefully considered.

There are some points of diagnostic importance which will aid in arriving at a rather accurate conclusion. In simple obstruction, rigidity and localized abdominal tenderness are not present. In loop obstruction where the bowel is strangulated by a loop of bowel either passing through a band of adhesion or becoming twisted upon itself in the nature of a volvulus, there is localized abdominal tenderness and some rigidity, as the distended loop of bowel contacts the parietal peritoneum. This is likewise true in intussusception of the terminal ileum into the ascending colon and to some extent with bands of adhesions to the anterior parietal peritoneum obstructing the bowel. When localized tenderness and rigidity are present in small bowel obstruction it may be stated that a strangulated loop of bowel is present and the blood supply is in danger.

While intestinal obstruction presents few or no early physical signs, their very absence indicates that there is no localized inflammatory process in any of the four quadrants of the abdomen. The colic is diffuse and periodic and differs from any other form of abdominal colic, which is usually localized in character and constant in type. The signs of a localized process are not present, as in acute inflammation of the appendix or gall bladder, or a perforated duodenal ulcer. The pain in obstruction comes in paroxysms, with intervals of relief. Peristalsis may be seen over the abdomen during the spasms of pain, and auscultation may reveal the increased sound of intestinal contractions. The abdomen presents a noisy rumbling sound during these paroxysms—borborygmus.

It must be remembered, as emphasized by Wangensteen and Goehl, that the passage of gas or movement of the bowels does not eliminate the possibility of obstruction. The bowel distal to the obstruction is unimpaired and may function normally, completely emptying itself of gas and feces. Wangensteen and Goehl stated that good results may be obtained by an enema, and unless this is kept in mind, a false security may result from a copious passage of gas or evacuation of the bowels.

Vomiting is dependent upon the duration and the level of the obstruction.

The very absence of early physical signs suggests the possibility of bowel obstruction and, in a patient who has had one or more abdominal operations, should bring to the surgeon's mind the possibility of an adhesive obstruction and cause him to seek the information which the radiologist can so accurately furnish.

The typical transverse pattern, described by Case, is not necessary for a diagnosis of small bowel obstruction. Collection of gas in the small bowel in the adult may be considered as synonymous with obstruction. In very small children, gas may be seen in the small bowel and be of no diagnostic significance. The presence of gas after obstruction is not a late development; it is seen early after the onset of the obstruction, usually being demonstrable without difficulty in four or five hours. The distribution of the gas in the small intestine is indicative of the probable type of lesion. Again let me emphasize that in simple obstruction it may be centrally located, with a transverse long axis, while in loop obstruction the dilated loops may assume no definite pattern, and proximal bowel distention is slow in developing. If the walls separating loops are thick, it signifies the presence of fluid or exudate. Gas in the large intestine is quite in contrast to gas in the small bowel, in that the long axis is vertical, the bowel wall is thicker, and haustral markings are present. The stepladder appearance of small bowel distention indicates advanced obstruction and is associated with a variable degree of abdominal distention. The gas is present and can be demonstrated long before distention and this particular pattern has developed. Thus, it may be said fairly accurately that the x-ray can make an early diagnosis of small bowel obstruction and that it can demonstrate the distribution of gas, and the location and probable nature of the obstruction.

From an abdominal roentgenogram, one can readily determine whether the distention is in the large bowel or the small bowel. If it is in the large bowel, it is usually a closed loop obstruction; the ileocecal valve prevents regurgitation into the ileum. If it is in the small bowel, the type and character of the distention depend upon the nature of the obstruction, and from the pattern of bowel distention the urgency of the situation becomes apparent.

In postoperative distention there may be a question as to whether a mechanical obstruction is present or a paralytic ileus. In the former event, the small intestines are distended, while in the latter there is distention of both the small and large bowel. A radiographic film shows the nature of the gaseous distention and helps to distinguish between the two conditions. If the obstruction involves the small bowel, it is distended and the colon is empty; in ileus, gaseous distention is present in both the small and the large bowel. Repeated films may be necessary to determine the certainty of an ileus. Consideration must also be given to the presence of a so-called silent and painless abdomen as a differential point in diagnosis.

A simple adhesive band producing proximal distention of the bowel results in no immediate vascular damage, and operation may be deferred until rehabilitation of the patient can be accomplished and intestinal decompression

established. A loop obstruction, volvulus or strangulation, on the other hand, demands immediate operative interference because of the danger of devitalization and bowel gangrene. With such an obstruction, the bowel is not observed assuming the transverse position but forming one or more distended loops, with no set pattern and with little or no proximal distention until the obstruction has been present for some time. The reason for the delay in distention of the proximal bowel is not understood, but it is probably due to the associated hyperemia and edema. Wangenstein and Lunch mentioned the altered state of the bowel proximal to the infarcted loop as a partial explanation.

The simple adhesive obstructions are the most common types involving the small intestine, and their presence can be detected early by radiologic study. The pattern is characteristic, and the sequelae of loss of electrolytes, of body fluids and distention are in relation to the extent and level of the obstruction.

CASE 1—M. I. entered the hospital with abdominal pain, periodic in character, and with moderate distention. Little or no fluid loss from vomiting had occurred. A recent operation had been performed elsewhere for an acute appendicitis. Recovery had been uneventful, without protracted hospitalization or abdominal drainage.

Obstruction was suspected because of the nature of the complaints, the absence of symptoms indicating any other type of colic or localized inflammatory process, and the presence of an abdominal operative scar, which always adds weight to the suspicion of small intestinal obstruction. An x ray picture (Fig. 1) revealed obstruction of the distal portion of the small bowel with only moderate proximal bowel distention. Favorable systemic and local conditions warranted immediate operation, which corroborated the x ray diagnosis of small bowel adhesive obstruction. The terminal ileum was constricted and angulated by a band of adhesion. Recovery was uneventful.

CASE 2—A similar condition is shown in M. H., a girl of 13 years who, six weeks previously, had an appendectomy for acute appendicitis, accompanied by drainage. Abdominal pain suggestive of obstruction prompted an x ray study of the gaseous distribution in the intestinal tract. This readily revealed a simple obstructive lesion of the terminal small bowel (Fig. 2). Again operation corroborated the x ray diagnosis. Recovery was prompt after an adhesive obstruction six or eight inches from the cecum was freed.

Loop obstruction presents an entirely different radiographic pattern and a distinct surgical urgency because of impending bowel gangrene.

CASE 3.—Fig. 3 shows the pattern of intestinal gas in a middle aged woman, S. B., who had previously had a total hysterectomy for a fundal carcinoma of the uterus. The x ray diagnosis was a loop obstruction of the small intestine, without proximal bowel distention, and immediate operation was advised. The possibility that obstruction was due to metastatic cancer was considered. At operation a loop obstruction with volvulus and gangrenous bowel, adhesive and benign in character, was found. Resection with side to side anastomosis was followed by normal convalescence. The clinical symptoms and radiologic film indicated a loop obstruction, which demanded immediate operation. The operative findings confirmed this conclusion. The resected specimen is shown in Fig. 4.

Small bowel obstructions frequently occur in association with inflammatory lesions within the abdomen and usually present the characteristic pattern of a progressive proximal bowel distention in which the viability of the bowel is not in jeopardy. In this type of obstruction it is not often necessary to interfere surgically, as the condition results from localized inflammation and edema which

narrow and constrict the adherent bowel to the point of obstruction, often in many places. The obstruction will usually disappear and the bowel again become patent, if the patient can be carried along by intestinal intubation and such rehabilitation methods as administration of fluids, saline solution, and transfusions until the inflammatory process has subsided.

Surgery is attended by great danger to the inflamed edematous bowel and may lead to extension of the infection. Intestinal decompression by the Miller-Abbott tube reduces distention and lessens the edema and hypertrophy proximal



Fig. 1 (Case 1)—Early small bowel obstruction from postoperative adhesive band. Note transverse position of small bowel distended coils, and gas seen in the right colon, rapid recovery followed operation.  
Fig. 2 (Case 2)—Early small bowel distention assuring transverse position. This is adhesive band type obstruction. Recovery followed operation.



established. A loop obstruction, volvulus or strangulation, on the other hand, demands immediate operative interference because of the danger of devitalization and bowel gangrene. With such an obstruction, the bowel is not observed assuming the transverse position but forming one or more distended loops, with no set pattern and with little or no proximal distention until the obstruction has been present for some time. The reason for the delay in distention of the proximal bowel is not understood, but it is probably due to the associated hyperemia and edema. Wangenstein and Lunch mentioned the altered state of the bowel proximal to the infarcted loop as a partial explanation.

The simple adhesive obstructions are the most common types involving the small intestine, and their presence can be detected early by radiologic study. The pattern is characteristic, and the sequelae of loss of electrolytes, of body fluids and distention are in relation to the extent and level of the obstruction.

CASE 1.—M. I. entered the hospital with abdominal pain, periodic in character, and with moderate distention. Little or no fluid loss from vomiting had occurred. A recent operation had been performed elsewhere for an acute appendicitis. Recovery had been uneventful, without protracted hospitalization or abdominal drainage.

Obstruction was suspected because of the nature of the complaints, the absence of symptoms indicating any other type of colic or localized inflammatory process, and the presence of an abdominal operative scar, which always adds weight to the suspicion of small intestinal obstruction. An x-ray picture (Fig. 1) revealed obstruction of the distal portion of the small bowel with only moderate proximal bowel distention. Favorable systemic and local conditions warranted immediate operation, which corroborated the x-ray diagnosis of small bowel adhesive obstruction. The terminal ileum was constricted and angulated by a band of adhesion. Recovery was uneventful.

CASE 2.—A similar condition is shown in M. II., a girl of 13 years who, six weeks previously, had an appendectomy for acute appendicitis, accompanied by drainage. Abdominal pain suggestive of obstruction prompted an x-ray study of the gaseous distribution in the intestinal tract. This readily revealed a simple obstructive lesion of the terminal small bowel (Fig. 2). Again operation corroborated the x-ray diagnosis. Recovery was prompt after an adhesive obstruction six or eight inches from the cecum was freed.

Loop obstruction presents an entirely different radiographic pattern and a distinct surgical urgency because of impending bowel gangrene.

CASE 3.—Fig. 3 shows the pattern of intestinal gas in a middle-aged woman, S. B., who had previously had a total hysterectomy for a fundal carcinoma of the uterus. The x-ray diagnosis was a loop obstruction of the small intestine, without proximal bowel distention, and immediate operation was advised. The possibility that obstruction was due to metastatic cancer was considered. At operation a loop obstruction with volvulus and gangrenous bowel, adhesive and benign in character, was found. Resection with side-to-side anastomosis was followed by normal convalescence. The clinical symptoms and radiologic film indicated a loop obstruction, which demanded immediate operation. The operative findings confirmed this conclusion. The resected specimen is shown in Fig. 4.

Small bowel obstructions frequently occur in association with inflammatory lesions within the abdomen and usually present the characteristic pattern of a progressive proximal bowel distention in which the viability of the bowel is not in jeopardy. In this type of obstruction it is not often necessary to interfere surgically, as the condition results from localized inflammation and edema which

CASE 4.—This case illustrates the value of conservative decompressive measures. W. H., a 16-year-old boy, presented the picture of an acute abdominal condition of several days' duration. The abdomen was boardlike but not distended; the pulse was fast, the temperature was elevated  $3\frac{1}{2}$  degrees, and the white blood count was 20,000. The patient was dehydrated and in very unfavorable condition for immediate surgery. An x-ray film showed no evidence of a pneumoperitoneum. Because it had been several days since the onset of the acute process, and because of the poor condition of the patient, conservative measures were adopted. A mass developed and subsequently a large appendical abscess was surgically drained and the appendix removed. Convalescence was stormy but progressive until the nineteenth postoperative day, when abdominal pain, periodic and cramplike in character, developed. Diffuse abdominal colic was followed by vomiting. Obstruction was suspected, and a roentgenogram of the abdomen (Fig. 5) showed rather extensive distention of the small bowel. A diagnosis of an inflammatory obstruction of the small intestines was made. The use of the Miller-Abbott tube (Fig. 6), adequate fluids, saline solution, glucose, and blood transfusions resulted in complete recovery after a secondary abscess spontaneously drained through the operative incision. After forty days of hospitalization, convalescence was complete and the patient was discharged.

In patients of advanced years in the absence of previous abdominal surgery, the possibility of a colonic lesion must be given careful consideration. This can be most effectively determined by barium enema. Such a lesion being excluded, some variety of small bowel obstruction must be considered. In Case 5, a barium enema excluded a colonic lesion.

CASE 5.—A man, aged 73 years, presented a three-day history of very slight abdominal pain and progressive abdominal distention. There had been no vomiting. There was increasing difficulty in bowel evacuation and none had occurred for five days. No operative abdominal incisions were present. An x-ray view of the abdomen showed small bowel distention (Fig. 7) and some excess amount of gas in the colon. A barium enema showed no colonic obstruction. A Miller-Abbott tube was passed successfully and the small bowel deflated (Fig. 8). A mass developed in the right iliac fossa and at operation a gangrenous appendix with abscess was found. Recovery was uneventful.

Mesenteric thrombosis is in reality an obstruction since peristalsis is abolished and bowel gangrene is imminent. The symptoms are different, as acute sudden pain may usher in the catastrophe. The x-ray picture shows gaseous distribution in the small bowel tract. With sudden onset, continuation of the pain and a gaseous distribution in the small intestines, abdominal exploration should be done. Segmental resection may be possible but too often the entire supply of the superior mesenteric artery is involved and nothing can be done.

CASE 6.—Mrs. H., ten days following thyroidectomy for long-standing hyperthyroidism and mild cardiac decompensation, on the eve of her departure from the hospital, was suddenly seized with severe persistent pain in the abdomen. An x-ray picture of the abdomen showed small bowel accumulation of gas. A tentative diagnosis of mesenteric thrombosis was made and abdominal exploration was done. The entire small bowel and the entire right colon were black. Subsequently at autopsy, a thrombus was found plugging the superior mesenteric artery. Nothing was found in the heart and no arterial sclerosis or atheroma was found in the arterial tree. The origin is unknown. Figs. 9 and 10 show the distention of the small intestines and the autopsy specimen of the involved segment of the superior mesenteric artery.

Intussusception presents two avenues for profitable use of the x-ray. First, it is most valuable in confirming the diagnosis suspected from the passage of

blood and mucus in the stools of an infant or small child who has abdominal colic and a palpable mass. Second, it is the only guide by which one may be certain of reduction by nonsurgical means. Only with the aid of a thin opaque enema can complete reduction be determined. Reduction may appear to be successful when in reality a segment at the ileum may remain intussuscepted. The completeness of reduction can be determined only by use of an opaque medium which shows the entire outline of the colon and cecum.

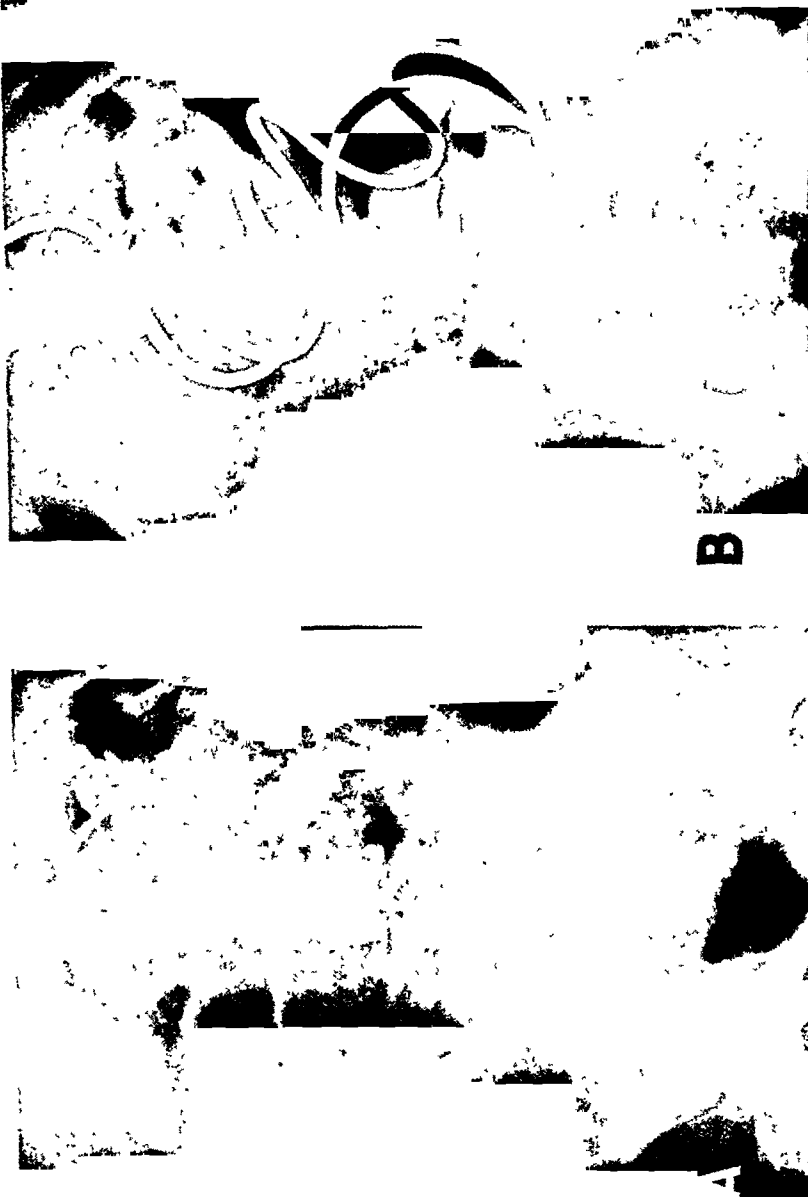


Fig. 5 (Case 4).—Small bowel obstruction following drainage of appendical abscess. Secondary abscess resulted in obstruction; recovery took place when abscess spontaneously drained through operative incision.

Fig. 6 (Case 4).—Small bowel intubation by Miller-Abbott tube; nonoperative recovery.

Fig. 11 shows an intussusception completely reduced by barium enema as demonstrated by a well-visualized cecum. Fig. 12 shows an intussusception of the ileum into the splenic flexure, requiring surgical reduction.

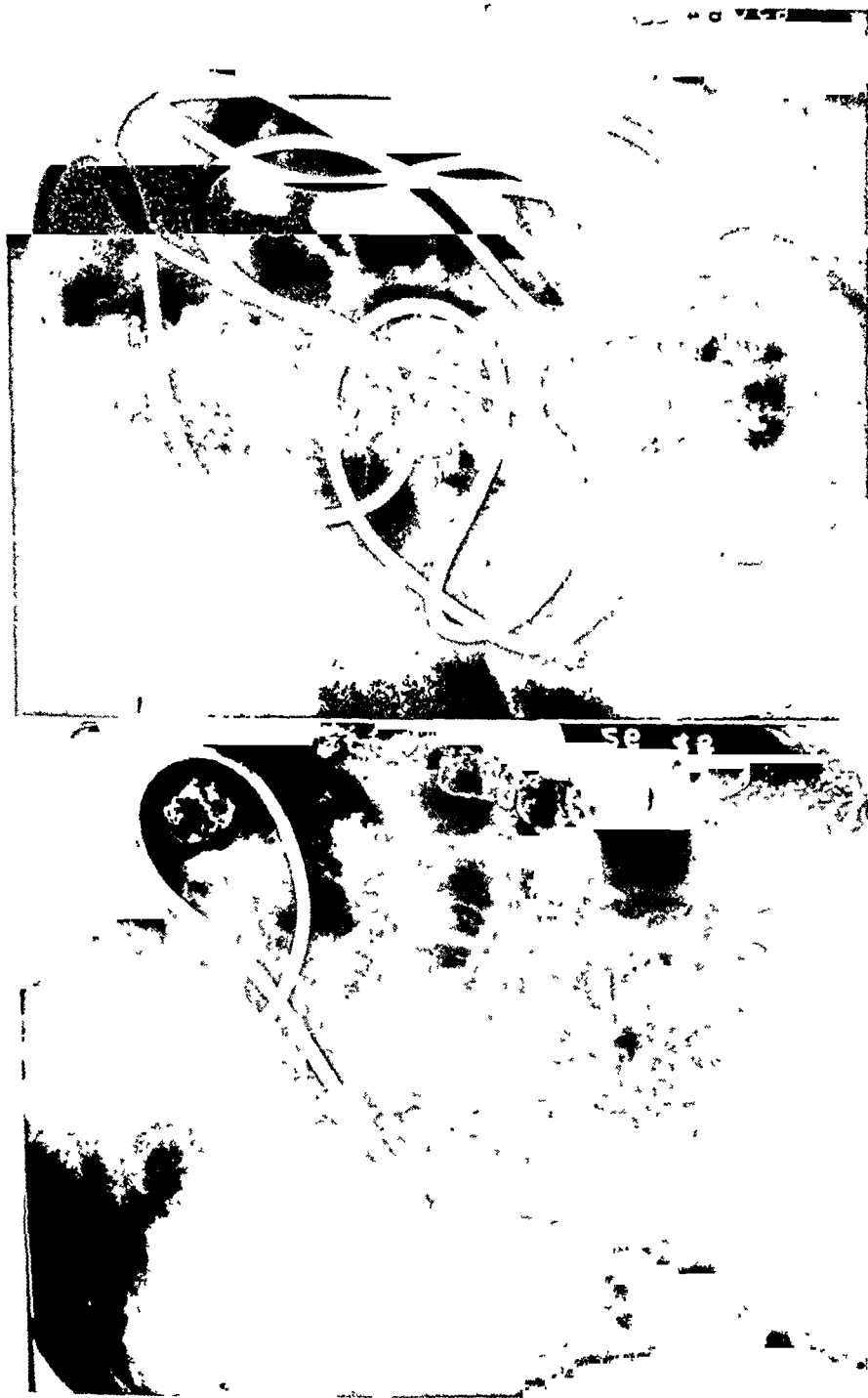


Fig. 7 (Case 5).—Note the intestinal pattern in which coils of dilated small bowel assume the transverse position; there is some excess amount of gas in the colon and an ilus due to acute appendicitis.  
Fig. 8 (Case 5).—The Miller-Abbott tube is shown well down in the bowel tract with resulting decompression.

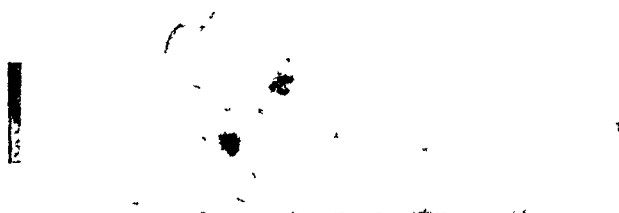


Fig. 9 (Case 6) —Small bowel distention from mesenteric thrombosis



Fig. 10 (Case 6).—Thrombus in superior mesenteric artery.

Intrinsic lesions obstructing the small bowel are due to the occasional obstruction from a gallstone or incomplete obstruction from a neoplastic lesion. The symptoms are those of biliary colic with subsequent bowel obstruction or progressive abdominal distress from a gradual occlusion of the lumen by the neoplastic growth.

Surgical management of stone obstruction depends upon the local condition of the obstructed bowel. If the stone can be dislodged it should be pushed upward to an uninvolved area of the bowel and removed through a longitudinal incision which is closed transversely. If edema and reaction prevent dislodgment of the stone, resection with anastomosis is advisable. Incisional removal through an indurated edematous bowel is hazardous. It will not heal.



Fig. 11.—Barium enema reduction of intussusception showing reduction to be complete.

Neoplastic lesions require resection when possible. If inoperable, anastomosis should be made between the proximal and distal limbs of the bowel around the lesion.

In partial obstruction much difficulty may be experienced in making a diagnosis from the radiographic film unless intermittent complete obstruction is present. Lockwood emphasized the advantage of opaque medium as an aid to diagnosis. Its significance centers around the rapidity of its progress through the intestinal tract. Any retardation of the barium or the detection of a mal-

formed loop is of great significance. Frequent roentgenograms are necessary to follow the barium in its intestinal advance.

#### INTESTINAL INTUBATION

The indications for the use of the Miller-Abbott tube in small intestinal obstruction are very definite. In the Research Hospital the procedure of passing the tube<sup>\*</sup> is the function of the radiological department.

The tube is indicated in simple adhesive obstruction with extensive proximal distention. It is valuable in early obstruction of a similar nature to prevent postoperative ileus and to hasten restoration of an already partially distended bowel. It is contraindicated as a preoperative measure in loop obstruction, in volvulus, or in strangulated obstruction where the viability of the bowel is in jeopardy. It may be valuable as a postoperative agent to prevent further distention and to hasten restoration of bowel tone.



Fig. 12.—Extensive intussusception of small bowel well into colon, not reducible by barium enema.

Although the Miller-Abbott tube has fallen into disrepute in many sections of the country, it is felt to be beneficial and can be applied in selected cases of intestinal obstruction.

The passage of the Miller-Abbott tube into the small bowel requires patience, along with a certain amount of skill. Much time can be saved by start-

<sup>\*</sup>Successfully accomplished by the radiologist, Dr. Ira H. Lockwood, and his associates, whose splendid cooperation is here acknowledged.

ing the intubation under fluoroscopic control. The procedure followed by Lockwood is as follows:

The patient is brought to the x-ray department with the necessary equipment. The tube is assembled and checked by the radiologist. If the patient is apprehensive, gags easily, or is restless, he is given sodium phenobarbital (1 to 4 gr. intravenously, depending upon his size) along with atropine (1/150 to 1/75 gr.). The depressant action of the phenobarbital on the gastrointestinal tract is felt to be much less than with opiates.

The tube is inserted into the stomach through the nose and pushed down along the greater curvature in an attempt to pass it through the pylorus. If the tube does not enter the duodenum immediately, the balloon of the tube is inflated slightly and is left in proximity to the duodenum. Peristaltic action of the stomach will guide the tube into the small bowel.

In patients with paralytic ileus and in moribund patients the instillation of hypertonic saline solution into the colon or an infusion of hypertonic saline solution into the vein will result in an increase in the peristaltic activity of the bowel. Only one word of caution—the reaction to the saline solution is sometimes violent. One must be sure that the tube is on its way down into the small bowel before the saline solution is administered, as perforation of the bowel may result without any means of decompression.

In this series of cases with the Miller-Abbott tube used as an adjunct in intestinal obstruction, a definite improvement was found in the condition of the patients in twelve to twenty-four hours.

In the past five years, forty-one patients have been operated upon for small bowel obstruction and several have been treated for obstruction due to an intra-abdominal inflammatory process and have recovered without operation.

Analysis of the forty-one operative cases was as follows:

29 small bowel obstructions from adhesive bands in which no resection was necessary

10 resections for devitalized bowel (no deaths)

2 cases of carcinoma of the small bowel, jejunum, and ileum, obstructive (operative recovery)

Three deaths occurred in this series:

1 postoperative intussusception (child, pneumonia)

1 postoperative secondary small bowel obstruction following cholecystectomy for stones; cause of death was intestinal obstruction, peritonitis

1 coronary thrombosis, following operation for small bowel adhesive obstruction

The Miller-Abbott tube was used in the nonsurgical treatment of those obstructions due to localized inflammatory processes. It was likewise used as an adjunct in more than one-half the operative cases, either as a preoperative or postoperative measure. Clinical and radiographic evidence of postoperative small bowel obstruction has frequently led to recovery by decompression with the Miller-Abbott tube without operation.



## SUMMARY

Classification of small bowel obstructions into strangulated hernias and those hidden within the abdominal cavity is discussed.

There is a discussion of strangulated hernia and reasons for immediate operation.

A description is given of the types of intra-abdominal obstruction of the small intestines and the immediate and remote effects of each.

There is mention of the indications for immediate or delayed operation.

Symptoms and signs of small bowel obstruction as distinguished from localized colic or inflammatory disease are emphasized.

Value of x-ray pictures in the diagnosis of obstruction and determining the type of obstruction is explained.

Value of x-ray is differential diagnosis between ileus and mechanical obstruction is discussed.

Indications are given for medical treatment of some type of intestinal obstruction where inflammation and infection are factors.

The diagnostic and therapeutic value of the x-ray in intussusception is mentioned.

Intestinal intubation, its indications, method of passage, and value are discussed.

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# FISSURES OF THE ARTICULAR CARTILAGE OF THE PATELLA

## OCCURRENCE IN MULTIPARTITE PATELLA

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THIS paper is presented to demonstrate that trauma or unusual stress to the knee may not only produce cracks and fissures of the articular cartilage of the patella<sup>1</sup> but may also affect in a similar manner the articular cartilage covering the ossicles of anomalous (multipartite) patellae of adults from 18 to 35 years of age. The interest lies first in the fact that the symptoms and signs encountered in these instances simulate to a certain extent those found in subluxations or tears of the semilunar cartilages and second, that those with anomalous patellae make up a high percentage of these cases. Since the osseous portion underlying the damaged articular cartilage was not fractured as demonstrated by radiographic examinations, there has been a ready tendency to overlook damage to the articular cartilage in the differential diagnosis of trauma to the knee. It appears that early recognition of tears or fissures in the articular cartilage of the patella and also that of an anomalous patella will aid materially in the plan of therapy and in better evaluation of the prognosis. As soon as more attention was given to this condition, the lesion was diagnosed in fifty-eight patients within a period of ten months. Twenty-three patients, or approximately 40 per cent of these cases, complained of symptoms in the knee for the first time. The duration of these symptoms was from several days to two months. In the other thirty-five patients, or approximately 60 per cent of the cases, who had recurrent symptoms of two or more months' duration, surgical intervention was performed in eleven instances including one with a bipartite patella. This inspection confirmed the clinical impression of the existence of fissures or cracks in the articular cartilage of the central portion of the patella in ten cases and that of the anomalous ossicle in the eleventh case.

The pathologic alteration in the cartilage of the patella may be readily suspected by an analysis of the mode of injury. Any mild to severe sudden force that tends to abut the patella against the femur with the leg in extension or flexion either directly or by torsion may initiate a fissure in the articular cartilage of the patella and may, in addition, occasionally similarly affect that of the contiguous femoral condyle.\*

Recurrent incomplete or complete subluxation of the patella either due to anomalies of the skeleton, laxity of the capsule or lateral ligaments, or muscle imbalance about the knee joint also predisposes to such changes in the articular cartilage of the patella. It is important to note that the articular cartilage of the patella is one of the thickest of the skeleton and is highly vulnerable to very mild direct or glancing blows. Furthermore, fissures may develop in the articular cartilage of the patella of certain young adults who have participated

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\*According to Owre<sup>2</sup> the site of stresses and strains upon the articular surface of the patella varies in flexion and extension. In flexion it is the lateral facet, and in extension it is the medial facet, of the patella which bears the respective impacts of the femur.

in unusual long hikes, marches, mountain climbs, or long periods of physical exercise without incurring any single definite pronounced local trauma. Newly inducted members of the armed forces who undergo extensive physical training are especially susceptible to such damage to the articular cartilage of the patella.

In this paper an attempt will be made to answer the following questions.

1. What are the symptoms and signs of fissures of the articular cartilage of the patella?
2. What are the significant radiographic findings?
3. What is the treatment and prognosis in the acute and chronic or recurrent forms?
4. What are the gross and microscopic findings of the involved articular cartilage?

#### CLINICAL FINDINGS

*Symptoms.*—Soon after an injury to the knee or after an unusual physical exertion, the patient may complain of sharp pains, instability, temporary locking, enlargement of the knee region, and inability to bear weight. The pain may be localized to the medial or lateral aspects of the knee or about the patella. Several days after the initial injury, the pain may become circumscribed to the patellar area, and it may be of such severity that walking or squatting is performed with great difficulty. Occasionally a click or sandpaper-like grating sound or vibration emanating from the knee may be heard or felt by the patient as the leg is actively flexed or extended.

In those patients with recurrent complaints lasting for two or more months following one or repeated injuries to the patella, enlargement of the knee region, temporary "locking," local pain, and loud crepitations are the foremost symptoms. While a swelling (effusion) may exist approximately from seven to thirty days following an initial mild trauma, it may recur at frequent intervals for many years in the severe or chronic types. Patients with prolonged recurrent symptoms may walk with the affected leg in fixed complete extension or in slight flexion in order to avoid pain and grinding crepitations in the knee.

#### PHYSICAL FINDINGS

Shortly following an injury to the patellar region, the examination often reveals an intra-articular effusion and generalized tenderness about the knee. Several days later the tenderness usually becomes circumscribed to the region of the patella and the effusion diminishes in volume. Passive rocking or percussion of the patella produces a tender reaction. With the aid of a stethoscope which is placed over the patella, high pitched cracking sounds are heard during active flexion and extension of the leg. Crepitation may also be felt by the examining hand as the patella is pressed onto the femur and passively displaced in the horizontal planes (*contact test*), or by active contraction of the quadriceps muscles with the leg in maximal extension. Pain is experienced during the latter procedure when mild manual resistance is applied to the superior pole of the patella (*resistance test*). It is interesting to note that in several cases in which the finding of subpatellar crepitation was equivocal, accentuation of this

sensation could be produced by flexing the thigh at an angle of 90 degrees at the hip joint while actively flexing and extending the leg (*stretching test*). During the painful stage, one often encountered temporary partial restriction of active and passive motion of the leg in both the range of flexion and extension, especially after a short period of weight-bearing. This finding may simulate that noted in a subluxed internal or external semilunar cartilage.

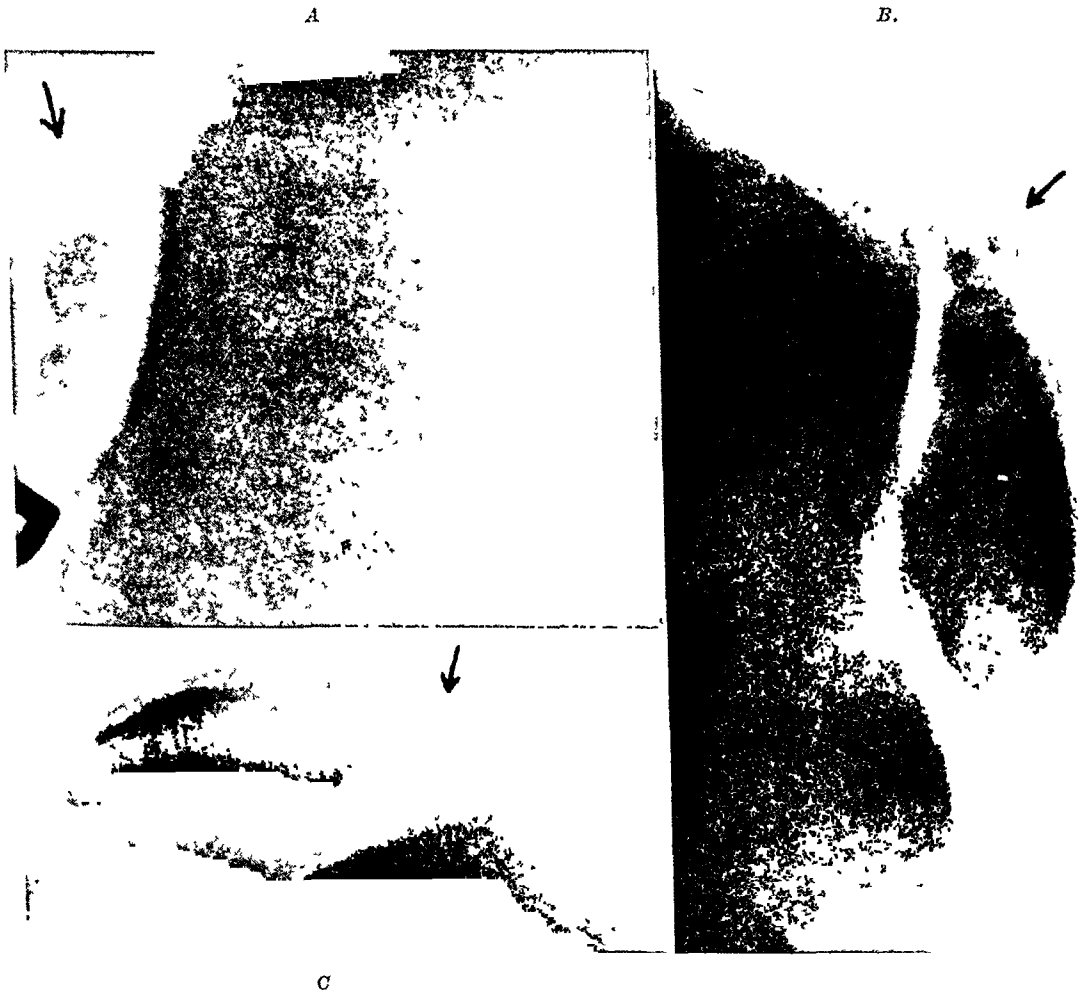


Fig. 1.—A, Note the three ossicles in the outer superior quadrant of the patella (quadrupartite patella.) B, Note the projection of these ossicles into the articular cavity beyond the normal articular surface (quadrupartite patella). C, Note the ossicles on the medial aspect of another patella (tripartite patella).

In those patients presenting a history of repeated injury to the patellar region, or those with long-standing symptoms following a single trauma to that site, examination revealed a definite thickening of the synovial tissues and frequently an increase in the volume of intraarticular fluid. Sometimes the pain over the patella was of such severity that the patient could not kneel and could walk only with his leg in fixed complete extension or in slight flexion. These objective findings were present in addition to the ones previously mentioned in the acute cases.

It should be stressed that fissures or cracks of the articular cartilage of the patella may be coexistent with tears of the internal or external semilunar cartilages or of the cruciate ligaments or relaxation of the posterior or lateral ligaments. When this occurs, additional signs such as tenderness over the lateral surfaces of the knee and instability of the tibia will be present which will mask to a certain extent those symptoms related to the damaged articular cartilage of the patella.

#### RADIOGRAPHIC FINDINGS

Radiographic examinations were made of both knees in the anteroposterior, lateral, and "jackknife" positions in each of the fifty-eight patients.<sup>3</sup> One may attach some importance to the fact that in this series of fifty-eight cases we noted eleven patients with anomalous patellae<sup>4</sup> (Fig. 1). The anomalies noted were that of ununited ossicles developed from accessory centers of ossification situated either in the outer superior quadrant or on the medial borders of the patellae.\*

TABLE I

<b>A. Bilateral Bipartite Patellae (5 cases)</b>	
	1 case, with acute symptoms
	4 cases, with chronic symptoms
	3 cases, each with symptoms in one knee
	2 cases, each with symptoms in both knees
	3 cases, with an ossicle in outer superior quadrant of each patella
	2 cases, with an ossicle on medial aspect of each patella
<b>B. Unilateral Bipartite Patellae (3 cases)</b>	
	1 case, with acute symptoms
	2 cases, with chronic symptoms
	3 cases, each with symptoms in the knee with anomaly
	2 cases, each with an ossicle in outer superior quadrant of one patella
	1 case, with an ossicle on medial aspect of one patella
<b>C. Unilateral Tripartite Patella (1 case)</b>	
	1 case, with chronic symptoms
	1 case, with symptoms in the knee with anomaly
	1 case, with ossicles in outer superior quadrant of one patella
<b>D. Bilateral Tripartite Patellae (1 case)</b>	
	1 case, with chronic symptoms
	1 case, with symptoms in one knee
	1 case, with ossicles on medial aspect of each patella
<b>E. Unilateral Quadpartite Patella (1 case)</b>	
	1 case, with acute symptoms
	1 case, with symptoms in the knee with anomaly
	1 case, with ossicles in outer superior quadrant of one patella

\*Surgical intervention in a case of bipartite patella of this series revealed the tears and cracks to exist in the cartilage of the ossicle and none in the articular cartilage of the body of the patella.

These patellae were in normal relationship to the femoral condyles in that they showed no evidence of fixed subluxation. Table I depicts some of the clinical and radiographic findings in the eleven cases of anomalous patellae.

Two other patients each of whom have had symptoms of pain, recurrent effusion, and crepitation for two years disclosed a circumscribed area of subchondral atrophy in the central portion of the patella of the affected knee. Otherwise the radiographic studies confirmed the clinical findings of increase in the volume of intra-articular fluid or thickening of the synovial tissues. No instances of osteochondritis dissecans, recent or old fractures of the body of the patella, postinfectious or infectious arthritis, or hypertrophic osteoarthritis were included in this series.\*

#### DIFFERENTIAL DIAGNOSIS

Difficulty is encountered when one attempts to differentiate tears of the articular cartilage of the patella from those of the opposing cartilage of the femoral condyles. They are both treated in a similar manner.

Free intra-articular bodies, polypoid synovial or fat pad tumors about the patella, osteochondromatosis or villonodular formations of the synovial lining may also produce effusion, subpatellar crepitations, and temporary lockings. Palpation usually reveals the presence of one or more bodies, and radiographs frequently show soft tissue shadows, or calcified or ossified masses either in the joint cavity or in the capsular tissues of the knee.

Symptoms and signs caused by chronic infections such as tuberculosis of the synovial lining or of the bones in the knee joint may infrequently simulate the physical findings produced by tears of the articular cartilage of the patella. Examination of the guinea pig inoculated with the synovial fluid aspirated from the knee joint and the radiographic evidence of atrophy or destruction of the articular surfaces of the bones of the affected knee may aid in the differential diagnosis.

Occasionally, a completely dislodged torn internal semilunar cartilage lying in the intercondylar fossa may to a certain extent parallel the findings caused by a cracked articular cartilage of the patella. The history of repeated "lockings" of the knee, the presence of localized tenderness over the medial surface of the knee in the region of the semilunar cartilage, especially of the posterior horn, and the persistence of effusion in spite of complete bed rest should make one suspicious of a torn and displaced semilunar cartilage.

Osteoarthritis, tangential fracture, and osteochondritis dissecans of the patella can be differentiated in most instances by radiographic examinations.

\*We did observe a patient who had suffered severe injury (fissure) to the articular cartilage of the patella several years before, who recently experienced a vertical undisplaced fracture through the body of the same patella. The radiographs revealed a fracture line but no other pertinent findings. The clinical course of this patient was striking and distinctly different from that of other patients with simple uncomplicated undisplaced fractures of the patella. Pain in the knee of the patient with the previous injury to the cartilage was severe for many weeks after the occurrence of the fracture and interfered with active and passive movements of the leg. This is in sharp contrast to a series of other patients with similar fractures without previous injury to the articular cartilage. Specifically a follow-up study of these patients with simple uncomplicated fractures of the patella six months after the injury showed absence of local pain and occasional presence of subpatellar crepitation on weight-bearing or on active repeated flexion or extension of the leg.

## TREATMENT

Patients examined after an injury to the knee or after participation in strenuous exercises of the types previously mentioned are treated by rest in bed for periods ranging from one to two weeks. The affected knee is covered with ice bags for the first few days to relieve pain and swelling. Subsequently, any type of dry or moist heat may be substituted to relieve the spasm of the thigh or leg muscles. Frequently traction is applied to the leg in order to overcome the spasm of the hamstring muscles.

No attempt should be made to flex forcibly or extend the leg either actively or passively during the acute painful stage, a period which may last from one to seven days. Exercises consisting of mild rhythmical contraction of the quadriceps muscles with the leg in maximal extension, however, should be encouraged as soon as possible after the advent of the injury. After the third week, or sooner if local pain is absent, active flexion and extension "resistance"

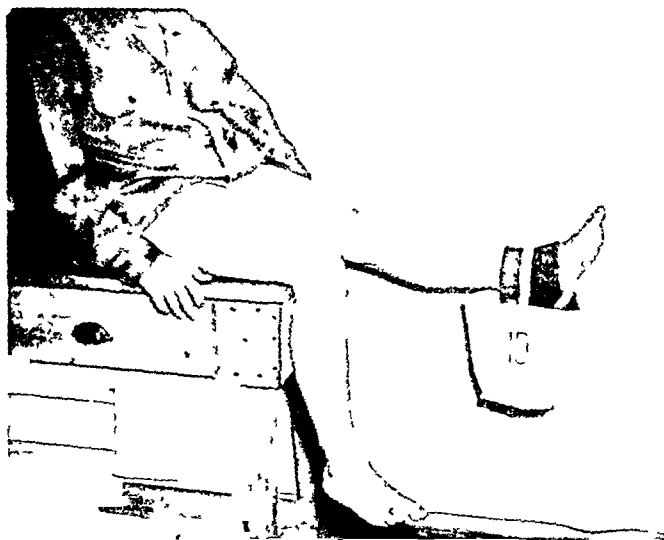


Fig. 2—Note the method of actively exercising the quadriceps apparatus of the leg.

exercises\* of the leg should be initiated and guardedly pursued. As soon as the power of the quadriceps muscles of the involved limb is approximately equivalent to that of the normal extremity, weight-bearing should be initiated. Special antilimping exercises as marching, walking, and dancing in cadence are stressed. No activities requiring excessive use of the knee should be encouraged, and only mild exercises should be pursued the first three or four months after the injury. We believe that graduated exercises to the quadriceps muscles will

\**Method.*—The patient is seated on the side of the bed in an attitude permitting flexion and extension of the leg (Fig. 2). A sack containing a known amount of weight, usually a minimum of three pounds and a maximum of twenty pounds, is hung on the ankle of the involved limb. Exercises consisting of repeated flexion and extension of the involved leg are pursued for four fifteen-minute periods during the day. Similar exercises are followed on the normal lower extremity. Once a day the maximal quadriceps power of the lower extremities is tested by noting the number of minutes that each limb can sustain uninterruptedly a known weight in the position of extension without pain or fatigue. The aim of these exercises is to develop the power of the extensor apparatus of the affected limb to a level equaling that of the normal one.

abort rapid progression of the fissures and cracks of the articular cartilage of the patella and at the same time develop the muscle tone of the limb. In a majority of cases, limited activities for three or four months will restore the knee to a serviceable but not to a normal joint.

Immediate surgical intervention is not indicated in the treatment of primary acute mild tears of the articular cartilage of the patella. When, however, there is a tendency for subpatellar pain, effusion, and crepitation to recur frequently or when these symptoms persist for total periods longer than two months in spite of rest and limited activity, arthrotomy should be pursued.

When limited areas of the patellar cartilage are involved as was the case in nine of the eleven instances in our series, we removed the central area of fissured articular cartilage down to the subchondral bone and made small openings into the underlying subchondral bone marrow. Excessive amounts of articular cartilage should not be removed, neither should the infrapatellar fat pad or the synovial lining be resected at the same time. The removal of intraarticular free bodies or a torn or subluxated semilunar cartilage is however, not contra-indicated. When the articular cartilage of the ossicle of an anomalous patella is involved, as was noted in one case, the underlying bone and cartilage of the ossicle were excised. For widespread cracked or split articular cartilage, removal of the entire patella is indicated. This was performed in a case of long-standing recurrent subluxation of the patella with marked secondary fissuring of the articular cartilage.<sup>5</sup>

Following an arthrotomy of the knee for the removal of fragments of torn articular cartilage, active contraction of the quadriceps muscles should be started soon after the surgical procedure. Moreover, the patient should attempt during the first fourteen days after the operation to elevate the entire limb without flexing the knee. These exercises strengthen the quadriceps muscles without imposing any unusual strain or irritation on the cartilage of the patella. Active flexion and extension and graduated "resistance" exercises of the quadriceps muscles should be initiated approximately fourteen days after the operation. The presence of pain in the patellar region is a contraindication for the continuation of flexion or extension exercises of the leg. Approximately six to eight weeks after the operation, or as soon as the quadriceps muscle power of the limbs is within normal limits, the patient should commence to bear weight and continue to do so if pain is minimal or absent. Activities which require excessive use of the knees should be restricted for a period of at least six months after the operation in order to permit the surgically produced defect in the articular cartilage to fill in with fibrous or fibrocartilaginous tissue.

When the patella is surgically removed, it is essential that active contraction of the quadriceps muscles be started soon after the operation. Active flexion and extension "resistance" exercises of the leg should be undertaken approximately seven days after the operation. Weight-bearing should not be stressed until the patient has accomplished almost full range of active flexion and extension of the leg without pain, and has almost fully developed the power of the quadriceps muscles.



*Follow-up Examination and Prognosis.*—In the acute cases including only those without previous involvement to the knees, the patients made an excellent recovery within two to three months after the initial trauma. These knees are for the most part highly susceptible to recurrence of symptoms and signs following very mild trauma or unusual exertion. Therefore, assignment to duty requiring excessive use of the knees should be avoided in view of possible recurrence of disturbance to the articulation.

In the chronic group there were seven patients in whom removal of torn and degenerated fragments of the articular cartilage of the patella was performed and there were two others in each of whom a torn internal semilunar cartilage was also removed. Follow-up examination of these nine patients six to eight months after the operation revealed free range of active and passive flexion and extension of the leg, loss of pain, absence of intra-articular effusion, and the presence of inconstant painless subpatellar crepitations. They were, however, unable to do very heavy duty without experiencing mild pains over the affected patella. Other patients with similar chronic disturbances in the patella whose onset of symptoms antedated entrance into the army were, depending on the severity of the symptoms and signs, either reclassified to perform sedentary duties or were separated from military service.

In the one patient (Case 10) in whom the ossicle and its cracked articular cartilage were removed from a bipartite patella, follow-up examination eight months after the operation revealed normal range of active and passive motion of the leg. The effusion and subpatellar crepitations which were noted prior to the operation were now absent. Yet in spite of good range of function the patient could not participate in strenuous activities for long periods as he experienced localized pains over the patella. He was permanently assigned to duty not requiring excessive or extensive use of the knees.

The excision of the patella in a case of recurrent subluxation of that bone with widespread fissures of the articular cartilage resulted in immediate loss of subpatellar pain and crepitation (Case 11). Follow-up examination six months after the operation revealed normal range of motion at the affected knee joint. Nevertheless, the patient had local discomfort after long hikes or mountain climbs. Therefore, he was assigned to duties limiting such strenuous activities.

#### PATHOLOGY

*Gross description.*—Surgical intervention in eleven cases gave us an opportunity to inspect the articular cartilage of the patella and the other structures in eleven knee joints. Except for the case of the bipartite patella, the central portion of the articular surface of each of the patellae, namely the medial facet and contiguous lateral facet, in an area approximately the size of a dime to a nickel was the site of the involvement. Here were numerous superficial or deep clefts, usually in a stellate design, which set off or enclosed one or more segments of shaggy yellow-white articular cartilage. In addition, flakes of cartilage loosely attached to the articular surface of the patella were noted in the vicinity of these fissures. The affected articular cartilage seemed to be easily separated

from the subchondral bone and was unusually fluctuant on pressure. Some of the detached flakes of cartilage were floating about in the synovial fluid or were embedded in the slightly reddened synovial tissues.

In the case of the bipartite patella, only the cartilage of the ossicle displayed a velvety shaggy yellowish-white surface with few superficial and deep fissures while that of the body of the patella presented no abnormal findings.

The patella, which was removed because of recurrent luxation, revealed on examination that its entire central portion measuring approximately the size of a nickel was the seat of deep stellate-shaped fissures (Fig. 3). Some of these clefts extended halfway into the depth of the cartilage and encompassed closely-set bundles of exposed fibrillar tufts.

In all eleven instances, one observed an edematous synovial lining in the knee and pannus formation over the periphery of the articular cartilage of the patella.

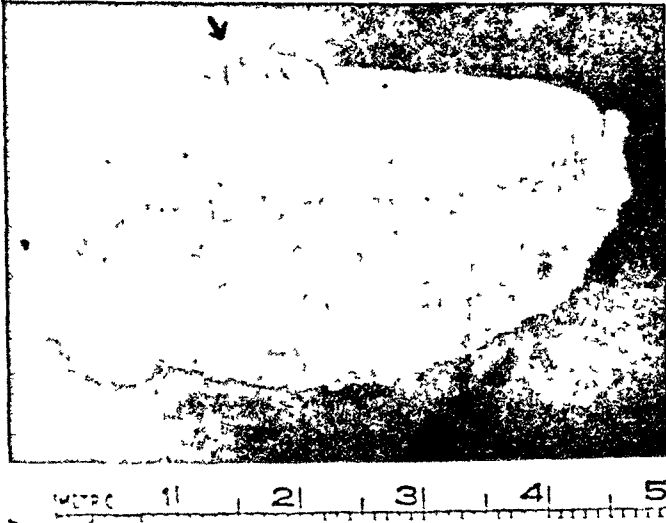
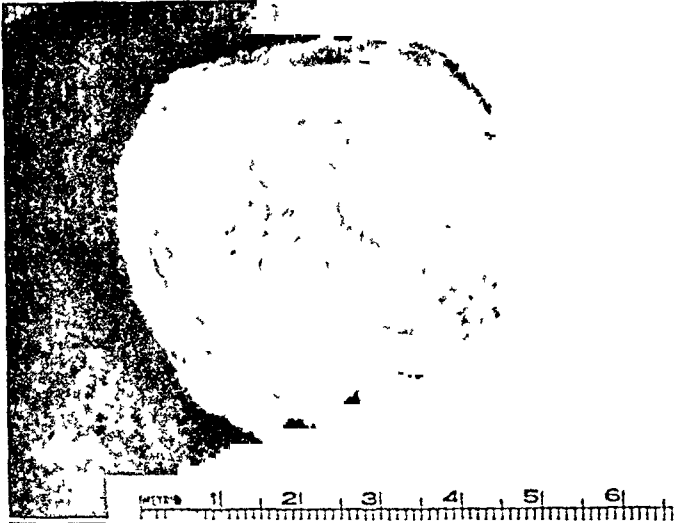
*Microscopic Findings.*—The striking feature was the partial loss of hyalin matrix, the secondary unmasking of the fibrils, and the presence of superficial and deep fissures in the articular cartilage. These abnormalities were especially prominent in the outer or tangential layer, and to a lesser extent in the contiguous zones of the articular cartilage. The flat cells normally situated in the outer or tangential layer were either absent or replaced by groups or nests of actively growing elliptical-shaped cells resembling those noted in fibrocartilage. Similar shaped cells, some filled with large amounts of chromatin, were also present in the depths of the cartilage especially adjacent to these abnormal fissures.

Evidence of partial repair as exemplified by the proliferating young cells on the articular surface and on the walls of the fissures was noted in the submitted portions of pathologic articular cartilage removed from the central portion of the patella. It appears that this meager attempt of healing of the cartilage was aided by the contiguous synovial fluid without benefit of granulation tissue.

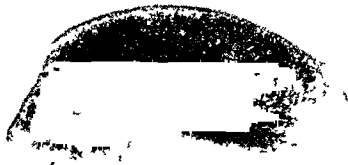
In the case of the bipartite patella, the articular cartilage of the ossicle was markedly degenerated showing partial loss of matrix, unmasking of the fibrils, and poor staining of the nuclei of the original cells. At the periphery of the ossicle was a thick layer of vascular fibrous tissue which bound it to the body of the patella. Some of these blood vessels invaded the rim of the articular cartilage of the ossicle but no other reparative processes were in evidence. The bone in the removed ossicle was for the most part necrotic and was slowly being replaced by living osseous tissue. There was very little active hematopoietic tissue in the marrow spaces in the ossicle.

The findings of the microscopic examination of the central fissured portion of the articular cartilage of the surgically removed patella were similar to those observed in the submitted pieces of cartilage from the previously mentioned cases. In spite of the protracted period of irritation to the patella caused by recurrent subluxation, there was no evidence of sclerosis or fibrosis of the subchondral zone.

A.



B.



C.

Fig. 3.—A, Patella surgically removed because of recurrent subluxations, note the fissures in the articular cartilage. B, Section of the articular cartilage of this patella reveals fissures and tufts. C, Lateral view radiograph of this patella; note the frayed articular cartilage.

## DISCUSSION

In order to comprehend the basis for the vulnerability of the articular cartilage of the patella, it is important to review briefly its histology and physical properties.

The articular cartilage of the patella of a young adult measures approximately from 4 to 6 mm. in height and is one of the thickest of the skeleton. It is relatively thickest in the central portion of the patella where the subchondral bone is slightly concave (Fig. 4). The articular surface is smooth, shiny, white, and fairly firm to the touch. On closer examination of the articular surface, one may discern without the aid of any magnifying lense, very fine grooves which extend from the superior to the inferior pole regions of the patella. These narrow shallow furrows are the result of the repetitive rotations of the femoral condyles on the patella.

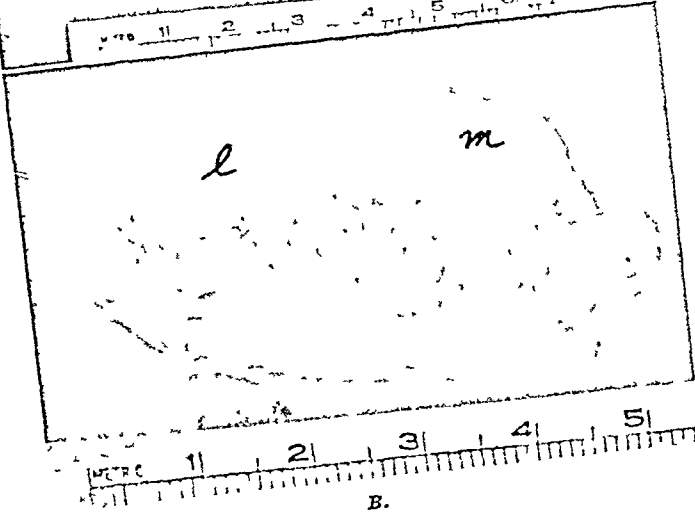
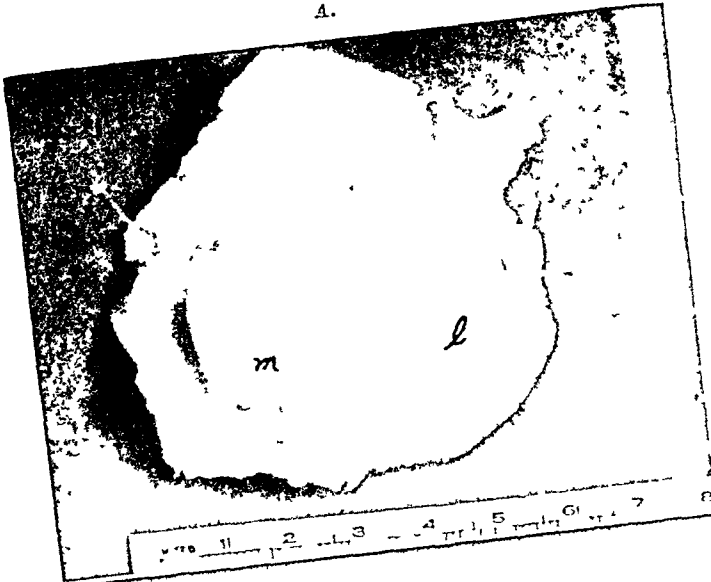
Normal articular cartilage is composed of cells and of very fine fibrils and interfibrillar hyalin matrix in such proportions that the fibrils are not clearly seen in the hematoxylin and eosin stained histologic preparations, but are observed microscopically with polarized light.\* These fibrils which form a network for the envelopment of the matrix follow more or less a fixed pattern (Fig. 5). They commence from the calcified or deeper portions of the matrix and extend in a vertical fashion through the columnar and transition zones to the superficial layers and curve to lie parallel to the articular plane to form the outer articular or tangential horizontal layer. These fibrils finally take another vertical course through the transitional and columnar layers and attach themselves to the calcified matrix or they may continue in the horizontal plane and terminate at the region of the capsule-periosteum reflection at the periphery of the cartilage.<sup>6</sup> The massing of these looped fibrils as they traverse the surface of the cartilage to return to the calcified matrix zone results in patterns<sup>7</sup> which are specific for the articular surface of each bone (Fig. 6).

In addition to the system of vertical fibrils one finds another set which encircles the nests of cells in the columnar layer. These circular fibrils act as shock absorbers by virtue of their possession of elasticity and compressibility.

As far as the cells are concerned, they are usually flat or elliptical in the outermost or tangential layer and almost resemble in shape those present in perichondrium. In the contiguous transition zone, the cells are somewhat more spherical or elliptical than those in the tangential layer. The outlines of the spherical cells may be slightly distorted by the contiguous fibrils which are in an oblique course en route to the superficial tangential layer. In the columnar layer, one notes the presence of nests of spherical cells in its proximal portion and columns of cells in its deeper segment. These columns of cells may extend into the calcified portion of the matrix.<sup>8</sup> Here, most of the cells appear necrotic as evidenced by poor staining of their nuclei and cytoplasm. Furthermore, it is of interest that the forementioned constituents of the articular cartilage do not

\*Normal articular cartilage is made up of the following four segments: (A) Thin outer tangential layer, flat cells and compact horizontal fibrils (Fig. 5); (B) thin transitional layer, elliptical cells and oblique fibrils; (C) thick columnar layer, nests and columns of cells, vertical and circular fibrils; (D) calcified matrix layer, columns of cells and vertical fibrils.

A.



B.



C.

Fig. 4.—A, Note the articular cartilage and the lateral (l) and medial (m) facets of a normal patella (post-mortem specimen). B, Section of the articular cartilage of this patella reveals its smooth glistening surface. C, Lateral view radiograph of this patella, note the thick articular cartilage and the concave subchondral bone.

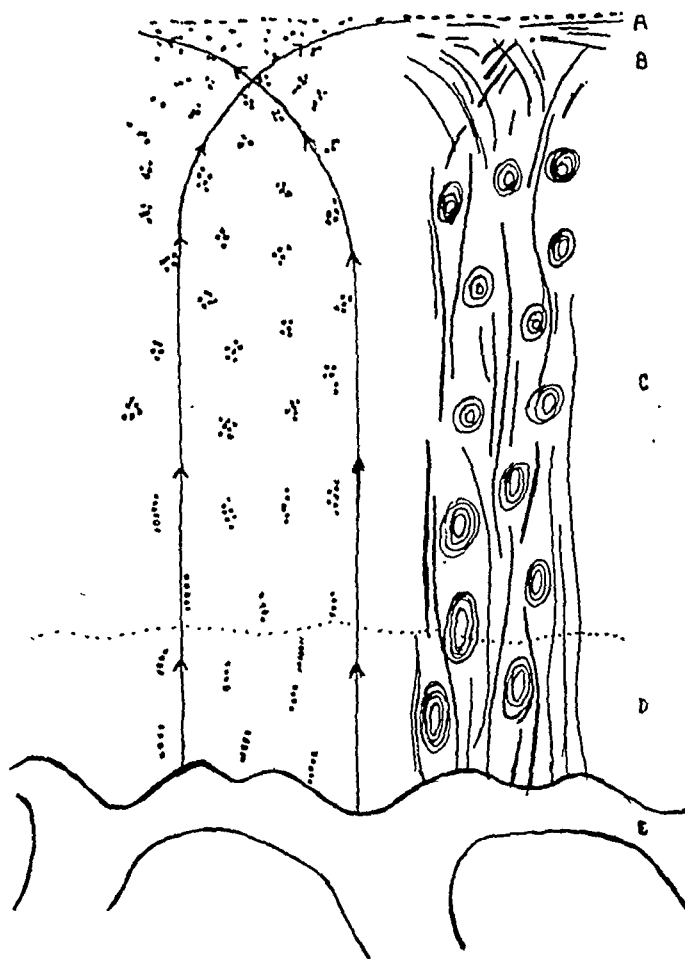


Fig. 5.—Diagram (after Policard<sup>8</sup>) to show the arrangement of the cells and the course of the fibrils in the articular cartilage as viewed microscopically. The arrows on the fibrils show approximately their course. *E* is the subchondral bone. See footnote in text (page 261) for explanation of the various segments of the articular cartilage.

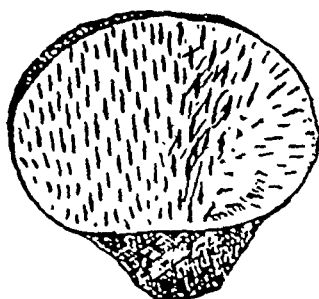


Fig. 6.—Diagram (after Hultkrantz<sup>7</sup>) to show the general direction of the bundles of fibers on the surface of the articular cartilage of the patella as seen macroscopically.

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# INGUINAL HERNIAS AND ALLIED DEFECTS IN NAVAL RECRUITS

## AN ANALYSIS OF 1,406 PATIENTS ADMITTED FOR SURGICAL TREATMENT

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**I**N THESE days it is only natural that surgical thought should be principally concerned with those great strides being made in the care of traumatic injuries. The first reports, now becoming available, from the Medical Corps of the Army and Navy in the combatant areas in all quarters of the world are superior to any previously recorded, and would have been entirely impossible only a few years ago.

However, during the first two years of World War II the task was primarily one of assembling, equipping, and training those forces to be used offensively on many fronts. A tremendous volume of corrective surgery was done in personnel by medical officers on the mainland during this period of preparation to remedy physical defects existing prior to enlistment and to bring the general physical condition of our forces to the highest possible level. In one Naval installation a series of 1,406 recruits with inguinal defects were admitted for surgical treatment during a twelve-month period. An analysis of this group of patients, with a discussion of certain technical details in their care and the management of complications, forms the basis of this report.

Tabulated in Table I are the various types of inguinal defects encountered in this series of 1,406 recruits in order of their frequency. The small number of patients with epigastric, incisional, and femoral hernias admitted are included to emphasize the fact that they were infrequently observed.

Uncomplicated inguinal hernias were by far the most common lesions for which patients were admitted for repair, the next most common being inguinal hernias with cryptorchidism, inguinal hernias with varicocele, and uncomplicated hydrocele in that order.

The incidence of inguinal hernias in men of military age examined during World War II is not yet public information. Coley<sup>1</sup> stated that 2 per cent of those examined during World War I were found to have such defects. It seems likely that with a more complete mobilization in this war, the incidence will be as high or even higher.

Coyer and Widder<sup>2</sup> recently reported an incidence of 3.71 per cent actual hernias in a large group of white male defense workers between 18 and 50 years of age, the figure being 9.2 per cent in a smaller group above 50 years of age.

In civilian practice indirect inguinal hernias are said to constitute approximately 93 per cent of all inguinal hernias while direct inguinal hernias will comprise from 2 to 10 per cent of any series, depending upon the average age of



TABLE I. INGUINAL LESIONS AND ASSOCIATED CONDITIONS EXISTING PRIOR TO ENLISTMENT

TYPE	NUMBER OF CASES	PER CENT SERIES
Inguinal hernia	1,073	76.4
Inguinal hernia with undescended testicle	97	6.8
Inguinal hernia with varicocele	66	4.6
Hydrocele, no hernia	56	3.9
Inguinal hernia with hydrocele	39	2.8
Varicocele (large), no hernia	37	2.7
Epigastric and incisional hernia	32	2.3
Femoral hernia	4	0.3
Inguinal hernia, varicocele, hydrocele	2	0.2
Total	1,406	100

the men examined. Coley<sup>1</sup> stated that femoral hernias, while representing 10 per cent of all hernias in both sexes, will be present in only 2.5 per cent of any series of male patients with hernia. In this period of observation only four recruits were admitted with femoral hernias for repair, an incidence of .3 per cent of the total group.

This series of men under discussion ranged in age from 17 to 35, the majority being between 17 and 24 years of age. Such a group represents a survey of young men in good physical condition, fit for vigorous military life except for the defects with which they were admitted (Table II). It is noteworthy that in the 1,073 recruits with uncomplicated inguinal hernias, indirect inguinal hernias were present in 91.8 per cent, direct inguinal hernias in 8.2 per cent, and bilateral lesions in 10 per cent. Direct hernias were seen with much greater frequency in those recruits between the ages of 25 and 35 years, being particularly common in those of short stature with a tendency to be overweight. As in the older age groups, direct hernias in these young men were usually bilateral. Unilateral inguinal hernias were consistently seen with greater frequency on the right side in an approximate rate of 6:4. This finding is in keeping with other reported experience.

TABLE II. UNCOMPLICATED INGUINAL HERNIA, SERIES OF 1,073 CASES

TYPE	NUMBER OF CASES	PER CENT SERIES
Inguinal hernia, indirect	986	91.8
Inguinal hernia, direct	87	8.2
Inguinal hernia, bilateral	108	10.0
Inguinal hernia, right	560	58.0
Inguinal hernia, left	405	42.0
Inguinal hernia, complete	307	28.6
Inguinal hernia, incomplete	766	71.4
Inguinal hernia, recurrent	20	1.8

In this series of cases the final diagnosis as to the completeness of a hernia was always made in the operating room. Hernias were considered to be complete in which a well-formed sac could be demonstrated extending down to the upper pole of the testicle or completely incorporating this structure. Since the majority of these indirect inguinal hernias were of the congenital type, one would expect a relatively high incidence of complete hernias. On the basis of the criterion listed, 28.6 per cent of this group of inguinal hernias were considered to be complete.

Twenty recruits were admitted for correction of recurrent indirect inguinal hernia, a previous surgical repair having been done prior to their entrance into the service. In every instance careful dissection at operation demonstrated a well-formed indirect inguinal sac varying in length from 4 to 12 cm. These findings confirm the established opinion that the essential step in the successful cure of indirect inguinal hernia in young patients is high ligation of the neck of the sac with complete removal of this structure.

A series of 298 cases was observed in which a hydrocele, varicocele, or an undescended testicle was present in the inguinal canal with or without an associated inguinal hernia (Table III).

TABLE III. HYDROCELE, VARICOCELE, AND UNDESCENDED TESTIS, WITH AND WITHOUT ASSOCIATED INGUINAL HERNIA, SERIES OF 298 CASES

TYPE	RIGHT	LEFT	BILATERAL	TOTAL
Hydrocele, no associated hernia	40	17	1	58
Hydrocele and inguinal hernia	22	17	1	40
Hydrocele, varicocele, inguinal hernia	0	2	1	3
Varicocele, no associated hernia	2	34	1	37
Varicocele and inguinal hernia	0	63	0	63
Undescended testicle, inguinal hernia	34	59	2	95
Undescended testicle, no inguinal hernia	1	1	0	2
Total				298

Hydroceles were noted more commonly without an associated hernia, and when this lesion was found alone, it was seen more than twice as frequently on the right side. Recruits with varicocele and inguinal hernia were admitted two times as frequently as were those with varicocele alone, since only those with large venous plexuses and definite symptoms were hospitalized for surgical correction in the absence of a hernia. The lesion was left-sided in all but two instances in these 100 cases in which a varicocele was present with or without an associated hernia.

Ninety-five recruits were admitted for repair of an undescended testicle with associated inguinal hernia. In only two cases was an inguinal testicle demonstrated in the absence of a patent hernial sac. The undescended testicle was found in an intraperitoneal position in only two instances, it having been arrested in its descent somewhere along the inguinal canal in the remaining ninety-five. In this age group the retained testicles were consistently found to be markedly atrophic, particularly those retained in the region of the internal inguinal ring.

Certain facts have been impressed upon us in making a clinical diagnosis of inguinal hernia in these patients. A complete inguinal hernia extending into the scrotum offers no problem in diagnosis, but an incomplete inguinal hernia or one with a long narrow sac may be extremely difficult to demonstrate on a single examination. We were repeatedly impressed with the accuracy of those medical officers who each day examined large numbers of incoming recruits in the reception center and referred those with inguinal hernias for surgical care. On several occasions we were unable to demonstrate conclusively a hernial sac on our first examination and after considerable debate have operated upon such an

individual admitted with a diagnosis of hernia only to demonstrate a complete well-formed sac in the canal. The logical conclusion is that these recruits when examined at the reception center had been on their feet for long periods of time, and had been subjected to various strains and exercises which greatly aided in demonstrating any hernial protrusion.

All patients in whom the diagnosis is questionable should be examined after they have remained on their feet for an hour or two during which time walking, stooping, and straining are encouraged. Both the erect and recumbent positions should be used in examination. We have found that the protruding sac can be demonstrated more frequently by straining, as in defecation, than by coughing. In the absence of a visible and palpable protrusion into the scrotum, our criterion for the diagnosis of an inguinal hernia has been the ability to palpate a definite sac within the external ring which fills, distends, and with straining can be definitely felt at the outlet of the ring. In general, the sac demonstrated at operation in questionable cases was larger and more complete than we expected to find in our early experience with this series of cases.

The surgical repair in these cases was done by four surgeons all using essentially the same technique. Spinal anesthesia was employed in the entire series, metycaine 10 per cent solution being used in 598 cases and novocain crystals or pontocaine in the 808 remaining cases. A total of ten partial anesthetic failures occurred, being much more common with novocain than metycaine.<sup>3</sup> However, in our hands metycaine produced an alarmingly high sensory anesthesia on several occasions which led to the routine use of novocain or its combination with pontocaine.

In the surgical care of the 1,073 patients with uncomplicated inguinal hernias a Bassini type of repair was used in 85 per cent of cases, a Ferguson in 7 per cent, the cord transplanted to the subcutaneous tissues in 7 per cent, and the McVay technique in 1 per cent. Before removal of the hernial sac, high ligation of its neck was routinely practiced but transfixion to the adjacent structures at the internal ring was not considered an essential step. Every effort was made to avoid tension in completing the hernial repair. The anterior edge of the lower rectus muscle sheath was frequently divided in a longitudinal direction 1.5 cm. medial to its lateral edge to permit more simple closure, when the conjoined tendon could not be readily sutured to the shelving edge of Poupart's ligament without tension. Both hydroceles and varicoceles were routinely exposed by an inguinal incision rather than through the upper scrotum because of the frequent association of hernias and the better wounds which resulted. Hydroceles were corrected by a modified "bottle operation" after as complete removal of the sac as was possible. Various types of operative procedures were employed for the correction of the large varicoceles. The most satisfactory results followed a removal of the anterior two-thirds of the venous plexus from the internal ring to the upper pole of the testicle, preserving the vas deferens and the spermatic artery.

In those patients presenting with an undescended testicle and inguinal hernia, the hernial sac was completely removed and every effort made to replace the testicle in the scrotum by lengthening the cord. A Ferguson herniorrhaphy was performed when scrotal replacement of the testicle was possible. Multiple staged procedures to replace a retained testicle in the scrotum were not practiced. When the inguinal testicle was small and atrophic and could not be replaced in the scrotum, orchidectomy was the procedure of choice when a normal testicle was present on the opposite side. Experience amply demonstrated that a testicle retained in the lower inguinal canal or over the symphysis pubes produced marked discomfort when recruits were subjected to a vigorous physical training program.

This group of young men in excellent physical condition, of similar age, and with comparable defects offered an ideal series in which to study wound healing with various suture materials. Chromic catgut, fine steel wire, and cotton thread were selected as the materials to be used under careful control.

Because of the known frequency with which hernial wounds become contaminated, a strict routine for preoperative preparation of the operative field was established during the first month of this study. The generous use of soap and water during the preoperative evening was the essential feature in the preparation of the inguinal areas; following this the field was covered with a sterile towel securely taped in place and not disturbed until the spinal anesthetic had been given. The inguinal regions were then cleansed with ether and painted with a standard antiseptic solution.

Chromic catgut in sizes No. 0 and 1 was used for repair of the hernia with No. 000 chromic or plain No. 0 for fine ties in one series of cases. A second series of cases was observed using fine steel wire and chromic No. 000 for ties. When cotton thread was employed No. 50 white was used for superficial ties and the hernial repair carried out with either No. 24 or 30 white thread. In a series of 239 consecutive cases, 1 Gm. of sulfanilamide powder was placed in the superficial fat before closure and its effect on wound healing noted.

For the first quarter of this study (300 cases) the dressings were changed on the third postoperative day and again on the seventh day after operation when the sutures were removed. In the remaining period (1,100 cases) the dressings were not disturbed until the seventh postoperative day unless specifically indicated, and pressure dressings utilizing two gauze rolls were routinely employed. All wounds were carefully graded and classified as having healed by primary union or as complicated grade A, B, or C. An "A" wound referred to a serum collection or small hematoma which in no way materially delayed convalescence or interfered with the wound integrity. Wounds classified as "B" evidenced a small stitch abscess which promptly responded to therapy in forty-eight to seventy-two hours. Type "C" wounds were those in which a frank infection developed, necessitating opening of the incision and producing a definite delay in convalescence and potential interference with the integrity of the wound.

The results of this study in wound healing are tabulated in Table IV. The wounds obtained using white cotton thread in sizes No. 50 for ties and No. 24

TABLE IV. WOUND COMPLICATIONS, SERIES OF 1,406 PATIENTS WITH INGUINAL DEFECTS REPAIRED WITH DIFFERENT SUTURE MATERIALS

MATERIAL	NUMBER OF CASES	"A"		"B"		"C"	
		NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT
Chromic No. 1, plain No. 0	165	31	18.7	1	0.6	9	5.4
Chromic No. 0, chromic No. 000(S)	114	8	7.0	1	0.8	3	2.6
Steel wire, chromic No. 000(S)	30	5	16.0	0	0.0	0	0.0
Cotton No. 24, No. 50(S*)	95	7	7.3	1	1.0	0	0.0
Cotton No. 24, No. 50	301	17	5.6	0	0.0	0	0.0
Cotton No. 24, No. 50 (P†)	701	14	2.0	3	0.42	7	0.27

Twenty-six of 82 type "A" wounds (32 per cent) due to hematomas.

\*S indicates 1 Gm. of sulfanilamide in wound.

†P refers to pressure wound dressing.

for the hernial repair together with a pressure dressing were so strikingly superior that this type of suture was routinely adopted for use in all general surgical procedures. Fine cotton suture material has the obvious advantages of low cost, ready availability, simple sterilization, and ease of handling. With its use the incidence of type "A" wound complications (serum or hematomas) was reduced to 2 per cent in the last 701 patients submitted to corrective inguinal procedures. The induration which usually characterizes a hernial wound closed with catgut, especially in the larger sizes, has been striking by its absence in this series of cotton wounds. In no instance has a draining sinus developed necessitating exploration of the wound to remove retained cotton knots. It is interesting to note that the introduction of 1 Gm. of sulfanilamide powder into the superficial fat of these wounds before closure, using both fine catgut and cotton suture material, consistently tripled the incidence of serum collections subsequently requiring evacuation.

The incidence of Type "B" and "C" wound complications referring to stitch abscesses or frank wound infections, respectively, was 1.4 per cent for this series of inguinal procedures. In the five wounds in which infection developed after closure with cotton, the subsequent healing time was quite comparable to that seen with a similar wound infection when catgut had been used as the suture material. We feel that cotton suture material is a very worth-while addition to our surgical armamentarium and will become increasingly popular with surgeons in the postwar era.

Postoperative pulmonary complications occurred in 2.4 per cent of this series of 1,407 consecutive inguinal procedures. Atelectasis, both lobar and lobular, and bronchiopneumonia were the most frequent chest complications encountered in the order named. In every instance there was a prompt and satisfactory recovery with appropriate therapeutic measures.

Postoperative urinary retention early presented itself as a complication of the first magnitude in this group of young men, in none of whom was organic urinary tract pathology present (Table V). In the first 301 operations, eighteen hours were allowed to pass following surgery before catheterization was resorted to if the patient was unable to void. Using ordinary conservative measures, the incidence of urinary retention in this group was 19.9 per cent. The use of the

TABLE V. POSTOPERATIVE URINARY RETENTION IN A SERIES OF 1,371 PATIENTS FOLLOWING INGUINAL PROCEDURES

NUMBER OF CASES	THERAPY	PATIENTS REQUIRING CATHETERIZATION	PER CENT REQUIRING CATHETERIZATION
301	C. M.,* 18 hours	60	19.9
202	C. M., prostigmine 1:4000	48	23.7
242	C. M., prostigmine 1:2000 (up patients)	10	4.1
240	C. M., sterile saline (up patients)	1	0.41
152	C. M., prostigmine 1:2000	3	1.9
65	C. M., sterile saline	3	4.6
169	C. M., 24 hours	2	1.2
1,371		127	9.2 Average

\*C. M., Conservative measures.

same conservative measures plus prostigmine 1:4000 for a total of eight doses had no effect in reducing the incidence of retention in a second group of 202 cases. Prostigmine 1:2000 solution was then adopted, one injection being given at 6 A.M. on the morning of surgery and seven injections following operation at four-hour intervals. In addition to this, twenty-four hours were allowed to pass following operation unless the patients were definitely uncomfortable and they were permitted to stand at the bedside to void if necessary. This latter procedure was considered entirely safe after the general adoption of cotton suture material for wound closure. With this routine the incidence of postoperative urinary retention fell abruptly to 4.1 per cent. This improvement was so dramatic that normal saline solution was substituted for the prostigmine solution without knowledge of the ward personnel, all other measures being continued. The results were even more striking, the incidence of retention dropping to .41 per cent.

Further series of cases were observed with the use of both prostigmine 1:2000 solution and normal saline solution, but again the patients were prohibited from standing at the bedside to void. In these two series the incidence of retention requiring catheterization was 1.9 and 4.6. A final group of 169 patients was observed in which no medication was employed, no patient was permitted out of bed, and twenty-four hours were allowed to pass in all cases before catheterization. The incidence of retention in this group was 1.2 per cent.

We concluded from this study that prostigmine was not primarily responsible for the reduction in the incidence of urinary retention in these young individuals.<sup>4</sup> The important factors were allowing twenty-four hours to pass before insisting that the bladder be emptied, permitting the sitting or standing position to void if surgically feasible, and providing good nursing care.

Unfortunately, it is impossible to have available the figures on recurrence in this series of inguinal defects subjected to surgical repair. To our knowledge, none of these patients have reported to date with a recurrence, although it is a well-established fact that these may be expected within the first year following surgical repair. Watson<sup>5</sup> stated that the recurrence rate for indirect inguinal hernias varied from 1 to 10 per cent, being lowest in the age group from 10 to 45 years, while the incidence of recurrence with direct inguinal hernias was from 10 to 20 per cent in the most experienced hands.

TABLE IV. WOUND COMPLICATIONS, SERIES OF 1,406 PATIENTS WITH INGUINAL DEFECTS REPAIRED WITH DIFFERENT SUTURE MATERIALS

MATERIAL	NUMBER OF CASES	"A"		"B"		"C"	
		COMPLICATION		COMPLICATION		COMPLICATION	
		NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT
Chromic No. 1, plain No. 0	165	31	18.7	1	0.6	9	5.4
Chromic No. 0, chromic No. 000(S)	114	8	7.0	1	0.8	3	2.6
Steel wire, chromic No. 000(S)	30	5	16.0	0	0.0	0	0.0
Cotton No. 24, No. 50(S*)	95	7	7.3	1	1.0	0	0.0
Cotton No. 24, No. 50	301	17	5.6	0	0.0	0	0.0
Cotton No. 24, No. 50 (P†)	701	14	2.0	3	0.42	7	0.27

Twenty-six of 82 type "A" wounds (32 per cent) due to hematomas.

\*S indicates 1 Gm. of sulfanilamide in wound.

†P refers to pressure wound dressing.

for the hernial repair together with a pressure dressing were so strikingly superior that this type of suture was routinely adopted for use in all general surgical procedures. Fine cotton suture material has the obvious advantages of low cost, ready availability, simple sterilization, and ease of handling. With its use the incidence of type "A" wound complications (serum or hematomas) was reduced to 2 per cent in the last 701 patients submitted to corrective inguinal procedures. The induration which usually characterizes a hernial wound closed with catgut, especially in the larger sizes, has been striking by its absence in this series of cotton wounds. In no instance has a draining sinus developed necessitating exploration of the wound to remove retained cotton knots. It is interesting to note that the introduction of 1 Gm. of sulfanilamide powder into the superficial fat of these wounds before closure, using both fine catgut and cotton suture material, consistently tripled the incidence of serum collections subsequently requiring evacuation.

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# Editorial

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## The Use of Chemotherapy in the Secondary Closure of War Wounds of Soft Parts

**A**N ANALYSIS of the experience of various surgeons with the secondary suture of war wounds of the soft parts reveals important discrepancies in technique. Failure to recognize these discrepancies has resulted in confusion concerning the use of chemotherapy as an adjuvant to the secondary suture of wounds of the soft parts.

The reported experience may be segregated into three main categories:

1. Secondary suture or skin grafting *at the time of removal of the first dressing* subsequent to initial surgery. Sulfonamide is given after initial surgery but is discontinued at the time of surgical closure of the wound. Healing without infection occurs in 90 to 95 per cent of cases.

2. Secondary suture or skin grafting of wounds dressed more than once after initial surgery. If no chemotherapy is given, healing without infection occurs in only 50 to 70 per cent of cases.

3. Secondary suture or skin grafting of wounds dressed more than once but patient given chemotherapy, usually sulfonamide, after secondary closure. Healing without infection occurs in 85 to 95 per cent of cases.

The surgeon who elects secondary closure at the time of removal of the first dressing accomplishes his objective with the least waste of time and effort and the results are as satisfactory as with any other method. Reliance is placed upon the clean surgical appearance of the wound as an index of the absence of infection.

The surgeon who elects secondary closure after two or more dressings of the wound has found it necessary to use chemotherapy, usually sulfonamide, to prevent infection. The ultimate results are comparable, but not superior, to the results attained by secondary closure at the time of the first dressing without subsequent chemotherapy.

Important clinical conclusions are permissible. The gross pathology of the wound is a reliable index of infection only when three to ten days have elapsed since the last dressing. Further, it is impractical to use bacteriologic cultures to determine the optimal time for wound closure. Contamination at the time of culture may not be revealed by the outgrowth of the coincidentally implanted organisms. The efficacy of sulfonamides in the prevention of infection in secondarily sutured wounds of the soft parts suggests that the most likely responsible pathogen is the beta hemolytic streptococcus. The bacteriologic studies of World Wars I and II support this conclusion. The efficacy of *systemically administered* sulfonamides in the therapy of impending streptococcal infection is clearly established.



partial early and a gradual late and usually incomplete return toward the preoperative state that limits the therapeutic effectiveness of the procedure. Clinical and experimental observations that might explain recovery phenomena will be considered first in three groups. General limitations of surgery of the sympathetic nervous system will then be discussed.

#### SYMPATHIETIC NERVE REGENERATION

Regeneration has been considered important as a limitation of sympathectomy since the studies of early investigators. Pyc-Smith<sup>14</sup> in 1887 reported recovery of control of the nictitating membrane, pupil, and temperature of the ear in a cat 110 days after removal of a portion of the left cervical sympathetic chain. Langley,<sup>15, 16</sup> Tsukaguchi,<sup>17</sup> Lee,<sup>3</sup> and others have established the ability of preganglionic fibers central to the superior cervical sympathetic ganglion in cats, dogs, and rabbits to regenerate. Functional preganglionic regeneration could be demonstrated by central stimulation in these experiments within three to eight weeks. Lee<sup>3</sup> brought out the remarkable ability of sympathetic nerves to bridge long defects. Regeneration occurred in one case 275 days after a one-inch separation of the cut ends of the cervical chain even though the sternomastoid muscle had been placed between the divided ends. Lee also reviewed the early literature of nerve regeneration and observed that vasomotor paralysis disappeared before sebomotor and pilomotor function returned. Tower and Richter<sup>18</sup> have demonstrated regeneration of divided preganglionic fibers central to the stellate ganglion in cats with return of skin resistance and skin action currents of the pads of the paws to normal. Hinsey, Phillips, and Hare<sup>19</sup> demonstrated preganglionic regeneration to the head and limbs of cats after various forms of sympathectomy.

Hollinshead and Finkelstein<sup>20</sup> demonstrated by histologic methods regeneration of the sympathetic nerve supply to the adrenal glands of cats as early as four months after sympathectomy. Haimovici and Hodes<sup>21</sup> demonstrated cardiac acceleration in completely sympathectomized cats and believed that this effect resulted from nerve regeneration to the adrenal glands. The phenomena of regeneration and partial recovery of sympathetic function after preganglionic sympathectomy of extremities in patients has been observed frequently by many surgeons and has been emphasized by Smithwick.<sup>22</sup> Kirgis and Ohler<sup>23</sup> described histologic evidence of regeneration after sympathetic ganglionectomy in cats. They observed functional regeneration to the eye but not to the leg or foot.

The ability of postganglionic sympathetic nerve fibers to regenerate has also been investigated. Tuckett<sup>24</sup> in 1896 obtained evidence of regeneration of postganglionic fibers from the superior cervical ganglion of a rabbit in 259 days. Machida<sup>25</sup> found regeneration as early as fifty-seven days and also noticed that vasomotor recovery preceded recovery of the pupil. Tower and Richter<sup>26</sup> found no evidence in the paws of cats of recovery of sweating or decrease of skin resistance that might indicate functional regeneration one to one and one-half years after division of the sympathetic fibers from the stel-

late ganglion. Hinsey, Phillips, and Hare<sup>19</sup> found no evidence of regeneration to the forepads of cats 236 days after removing the thoracic chain from the stellate through the eighth thoracic ganglion. Kilvington and Osborne<sup>27</sup> reported return of vasomotor reflexes as determined by the plethysmograph 205 days after section of the sciatic nerve of dogs. Trotter and Davies<sup>28</sup> observed recovery of sebomotor and pilomotor function six to eight months after peripheral nerve section performed upon themselves. Kredel and Phemister<sup>29</sup> have demonstrated varying degrees of restoration of vasomotor, pilomotor, and sebomotor function in pedicle skin flaps in which nerve and blood supply had been completely severed in stages. Recovery of central vasomotor tone and of a vasoconstrictor mechanism capable of response to central stimulation has been reported in completely sympathectomized dogs.<sup>30</sup> Histologic evidence of sympathetic nerve regeneration that might explain the incomplete vasomotor recovery observed was described. Additional unpublished studies by F. E. Kredel, H. Wilson, and D. B. Clark of blocks of tissue removed from the scar of excision of the sympathetic chain of these dogs have demonstrated that regenerating fibers leave the divided sympathetic rami and enter and follow along the scar. Sympathetic fibers were few and scattered in the first few weeks. However, one year or more after sympathectomy, definite nerve bundles coursed along through the scar. Simmons and Sheehan<sup>31</sup> demonstrated by ulnar nerve block evidence of regeneration in patients having a late relapse after ganglionectomy or preganglionic sympathectomy performed for acrocyanosis, Raynaud's disease, or scleroderma of the upper arm.

These reports and many others demonstrate that nerve regeneration and a varying amount of recovery of function may occur after division or excision of sympathetic nerves and ganglia. While this process may limit the enduring effectiveness of regional or total sympathectomy it probably does not explain the early partial recovery of vascular tone. Two factors that play a role in the early recovery will next be considered.

#### INCREASED IRRITABILITY OF SMOOTH MUSCLE AFTER SYMPATHECTOMY

An increased responsiveness of denervated smooth muscle to blood-borne vasoconstrictor or vasodilator substances might limit the early effectiveness of sympathectomy. Bernard<sup>32</sup> in 1852 divided the cervical sympathetic chain below the superior cervical ganglion in animals and observed turgescence of blood vessels and increased warmth in the denervated area. He recognized that the enlargement of the blood vessels diminished within several hours and might not be visible one day after nerve section but that the warmth persisted several months and was maintained during exposure to cold. He later observed<sup>33</sup> that the paralytic effect of removal of the superior cervical ganglion was more rapid, more intense, and greater than that produced by simple section of the cervical sympathetic chain and that it might last at least one and one-half years in the dog.

Degeneration of postganglionic sympathetic nerve fibers was employed by Lewandowsky<sup>34</sup> and Langley,<sup>35</sup> who excised the superior cervical ganglion, and by Brodie and Dixon,<sup>36</sup> who div

demonstrate that adrenalin had a peripheral action. Meltzer and Meltzer<sup>37</sup> studied the circulation of the rabbit's ear after unilateral resection of the sympathetic chain or the superior cervical ganglion. They observed that the constriction of the blood vessels produced by intravenous adrenalin began later, developed more slowly, and lasted longer in the denervated than in the opposite ear. They also observed<sup>38</sup> that dilatation of the vessels of the normal ear and constriction of those in the sympathectomized ear followed moderate amounts of adrenalin introduced subcutaneously. They concluded that varying degrees of sympathetic vasoconstriction and vasodilatation of central origin modify the peripheral action of adrenalin in the normal ear and that the phenomena observed in the sympathectomized ear represents the peripheral action of adrenalin freed from these central influences.

An essential difference between division of the cervical sympathetic chain, preganglionic sympathectomy, and excision of the superior cervical ganglion, ganglionectomy, was described by Meltzer and Auer<sup>39</sup> in rabbits and Meltzer<sup>40</sup> in cats. They observed that subcutaneous adrenalin had no effect on the normal pupil or upon the pupil denervated by preganglionic sympathectomy but that it produced maximum dilatation of the pupil denervated by ganglionectomy. This effect was first evident twenty-four to forty-eight hours after ganglionectomy and continued during a three and one-half month period of observation. Elliott<sup>41</sup> extended these studies to include the smooth muscle of blood vessels and noted that the increased irritability persisted at least ten months. He also noticed that some degree of increased irritability followed preganglionic sympathectomy. He stated, "This, then, is true for all the muscles thrown into contraction by adrenalin, that after decentralization (i.e., degenerative section of the preganglionic sympathetic nerves), and still more clearly after denervation (degenerative section of the post-ganglionic sympathetic nerves), they contract in the presence of adrenalin alike with greater irritability and persistence."

Dale and Richards<sup>42</sup> demonstrated that the blood vessels of cats were rendered abnormally sensitive to the vasodilator action of histamine and acetylcholine as well as to the constrictor action of adrenalin by complete degeneration of their nerve supply.

Rosenbleuth and Cannon<sup>43</sup> studied the effect of sympathin on the nictitating membrane of the cat after removal of the superior cervical ganglion and determined that contraction would occur only after "sensitization" of the animal by cocaine injection. Hempel<sup>44</sup> also studied adrenin and the nictitating membrane of the cat and observed that the increased response following section of the cervical sympathetic chain is about one-half as great as that which follows denervation by ganglionectomy. He reviewed the theories advanced to explain the increased "sensitivity" and favors the Rosenbleuth proposal that an increase in permeability of the denervated cells after sympathectomy is responsible.

Freeman, Smithwick, and White<sup>45</sup> employed intravenous adrenalin and insulin hypoglycemia in patients and observed an abnormal lowering of skin

temperature that developed six or eight days after removal or alcohol injection of the sympathetic ganglia. This effect was also observed during insulin hypoglycemia in rabbits and cats. Removal of one adrenal and denervation of the other prevented the vascular constriction which usually accompanied hypoglycemia in animals. Smithwick, Freeman, and White<sup>46</sup> considered the possible relationship of this "hypersensitivity" to the recurrence of vascular spasm in Raynaud's or vasospastic disease that often occurred after upper arm sympathetic ganglionectomy. Four patients treated by cervicodorsal ganglionectomy demonstrated a marked degree of vasospasm following intravenous epinephrine. Three of these, ten days, twenty-two days, and ten months, respectively, after operation, had a marked clinical recurrence of spasm, and one three months after operation had no clinical recurrence. Two patients after lumbar ganglionectomy had marked and moderate spasm with epinephrine, although clinical recurrence was slight or absent at twenty-two days and at ten months. One other patient described had an incomplete sympathectomy and three had no note concerning clinical recurrence. These authors concluded from these limited clinical studies that hypersensitivity to circulating epinephrine may constitute an important source of unsatisfactory results of sympathetic ganglionectomy for Raynaud's disease.

Grant<sup>47</sup> studied the vasomotor reaction of the rabbit's ear to changes of room and body temperature, nervous and muscular activity, and adrenalin. Increased responsiveness of denervated vessels developed during five to seven days and then remained constant during nine-, thirteen-, and fifteen-month periods of observation. One rabbit, however, regained constriction of the ear vessels between thirteen and eighteen months after excision of the superior cervical and stellate ganglia. Preganglionic sympathectomy was also observed to produce an enhanced responsiveness although less than that produced by removal of the ganglia. The reactions of the normal and the denervated ears were not altered by adrenalectomy or by removal of the pituitary body. Grant believed, therefore, that under conditions of nervous and muscular activity an adrenalin-like substance, probably not sympathin, circulates through the blood from some unknown source. This substance was thought to play a role in maintaining normal vascular tone and body temperature and in stimulating the increased responses observed in denervated vessels.

White, Okelberry, and Whitelaw<sup>48</sup> made further observations on the denervated rabbit's ear and on the hands of two monkeys. Following denervation of one hand of the monkeys by ganglionectomy 1 c.c. of 1 to 1,000 epinephrine produced a surface temperature lowering from 86 to 74.5° F. in one animal and 0.25 c.c. produced a fall from 88.5 to 81.5° F. in the other. The temperature of the control hands was not changed. In addition the spinal roots from the fourth thoracic vertebra through the tenth were divided on the side of the control hand of one monkey. Epinephrine (0.25 c.c.) later produced a lowering of the temperature of this hand from 89 to 85° F. and a lowering of the hand denervated by ganglionectomy from 87.5 to 79.5° F. These authors believed that this "sensitization" phenomenon accounts for re-

currence of vasospasm. They also believed that since leg denervations are usually preganglionic this may explain the better effects of sympathectomy of the leg than the arm of patients with Raynaud's disease.

Ascroft,<sup>49</sup> working in the laboratory of physiology at Yale in 1935 and 1936, studied the reaction to local cold and to adrenalin in twelve monkeys that had undergone cervicothoracic ganglionectomy and eight that had preganglionic sympathectomy. Nine of the twelve reacted to local cold as well as did the normal limb; two reacted more intensely than did the normal; and in only one did a good degree of vasodilatation persist. Each of the eight that had preganglionic sympathectomy developed less reaction to cold than did the normal limbs. Adrenalin "sensitization" occurred in all of the sympathectomized limbs. After preganglionic sympathectomy the reaction to adrenalin was three times as great as in the normal limb and after ganglionectomy it was ten times normal. Ascroft also noted an opposite order of "sensitization" for pitressin and ephedrine. Preganglionic sympathectomies produced more "sensitization" to these drugs than ganglionectomies. Denervation of one adrenal gland and removal of the other in two monkeys did not prevent abnormal response to cold of hands denervated by ganglionectomy. This observation agrees with that of Grant<sup>47</sup> and indicates that the adrenal medulla is not solely responsible for all of the observed "sensitization" phenomena.

Freeman, White, Smithwick, and others quoted have stated that preganglionic sympathectomy might be more beneficial than ganglionectomy in the treatment of patients with vasospastic peripheral vascular disease. Telford<sup>50</sup> and Smithwick<sup>51</sup> in 1935 independently performed preganglionic sympathectomies rather than ganglionectomies for vasospastic diseases of the arms of patients. Reports of these authors were encouraging. Lewis<sup>52</sup> presented six patients treated by preganglionic sympathectomy for Raynaud's disease of the hands that early demonstrated clinical improvement. In five of the six, vasospastic attacks recurred spontaneously or could be produced by cold and occlusion. He concluded that these attacks are related to some local fault of the blood vessels since central vasoconstrictor nervous influences had been eliminated by the sympathectomy and since sensitization by ganglionectomy or preganglionic sympathectomy of the blood vessels of arms of patients that have no pre-existing vasospastic disease does not produce Raynaud's disease or similar clinically significant sensitization phenomena. Simmons and Sheehan<sup>51</sup> emphasized the significance of this local fault in the early relapse following sympathectomy and the importance of nerve regeneration in the late relapse. Among thirty-three complete ganglionectomies, early relapse occurred in nine, late relapse in twenty, and no relapse in four. Among twenty-eight preganglionic sympathectomies, early relapse occurred in four, late relapse in seventeen, and no relapse in seven. Longer observation of this second later series might have further altered the group proportions. Ulnar nerve block by novocain gave increased temperature of the little finger in the patients with late relapse that in view of control studies would seem to indicate regeneration.

Late relapse usually occurred six to nine months after ganglionectomy and as early as three months after preganglionic sympathectomy. White<sup>53</sup> summarized the surgical opinion developed during the first three or four years of clinical use of preganglionic sympathectomy. He stated that most surgeons agree that ganglionectomy no longer should be done because of the associated increased sensitivity of the smooth muscle of the arterioles.

Fatherree and Allen<sup>54</sup> and later Fatherree, Adson, and Allen<sup>10</sup> after many carefully controlled clinical experiments disagreed with the clinical observations and conclusions of Smithwick, Freeman, and White quoted previously. The first report<sup>54</sup> controlled the experimental conditions necessary for an accurate evaluation, by skin temperature observations, of the effect of injecting epinephrine. They demonstrated that the vasoconstrictor effect of epinephrine varies widely in normal individuals and is not necessarily exaggerated in patients with Raynaud's disease. Their second report<sup>10</sup> demonstrated that sympathectomy of the upper extremity of man by removal of the ganglia (postganglionic sympathectomy) does not produce nearly as great a "sensitivity" of smooth muscle as it does in monkeys. Preganglionic sympathectomy and postganglionic section (ganglionectomy) of the hand of patients each effected a decrease in cutaneous temperature in response to standard doses of epinephrine that was approximately twice that observed before operation. These authors concluded: "The problem of unsatisfactory results that occasionally follow operation for Raynaud's disease of the hands has not been satisfactorily solved by a study of sensitivity of digital arterioles to epinephrine." This conclusion is in agreement with the opinion of many surgeons and myself that these unsatisfactory results have not been materially solved by operations employing the preganglionic sympathectomy technique.

These reports of increased irritability of smooth muscle after sympathectomy indicate that sensitization phenomena develop shortly after any form of sympathectomy, reach their maximum within two weeks, and then persist unless regeneration occurs. These phenomena may limit the early effectiveness of any sympathectomy during periods of local cold or during circulation of adrenalin and adrenalin-like substances in the blood stream. It would seem evident now that ganglionectomy, as described for the upper arm by Adson and Brown<sup>55</sup> and by Gask,<sup>56</sup> is associated with less risk of regeneration, but more of "sensitization," while preganglionic sympathectomy, as carried out by Telford<sup>50</sup> and Smithwick<sup>51</sup> involves greater risk of regeneration and less of "sensitization." Further considerations related to the decision between these two types of operations will be described.

#### RECOVERY OF INTRINSIC PERIPHERAL VASCULAR TONE AFTER SYMPATHECTOMY

The inherent ability of the smooth muscle of blood vessels to maintain an independent tone probably limits the early and late effectiveness of sympathectomy more than any other single factor. The finer arteries and arterioles containing smooth muscle, and the much greater capillary bed, are largely

currence of vasospasm. They also believed that since leg denervations are usually preganglionic this may explain the better effects of sympathectomy of the leg than the arm of patients with Raynaud's disease.

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for many hours in others. These and other experiments dealing with the proprioceptive reflex mechanisms that regulate blood pressure thus indicate that central or peripheral reflex activity modulates peripheral vascular tone but does not entirely maintain it and cannot entirely overcome it even by active vasodilatation.

Studies of circulation and blood pressure in animals after destruction of the thoracic and lumbar spinal cord, or after total paravertebral sympathectomy, also demonstrate that the peripheral vascular bed maintains and improves tone after denervation. The cord destruction experiments also yield observations relative to the circulation after a preganglionic sympathectomy of the entire body. The complete paravertebral sympathectomy experiments offer comparable studies on the effects of sympathetic ganglionectomy.

Hermann, Morin, and Vial<sup>64, 65</sup> have reviewed the effects of cord destruction. They demonstrated by acute experiments that ascending destruction of the spinal cord to progressively higher levels effects appreciable lowering of blood pressure only after the seventh thoracic spinal segment is reached. Further destruction of the remaining upper thoracic segments lowered the pressure to values around 50 mm. Hg. Destruction of the entire thoracic and lumbar cord was associated with a relatively normal blood pressure even though chronic experiments were continued up to one year and fifty-three days. Normal values returned within one day, or two, of the operation and were maintained. These animals with preganglionic sympathectomies of the entire vascular bed, produced by cord destruction, were extraordinarily sensitive to small doses of hypertensive pharmacologic products, such as adrenalin. These authors discussed the possibility that either a sensitization to adrenalin liberated by humoral stimulation of the denervated glands or a peripheral nervous tone arising in the decentralized sympathetic ganglionated chains might partially account for the maintained peripheral resistance.

Removal of the paravertebral sympathetic chains was first performed upon cats by Cannon and associates.<sup>66</sup> The effects of this procedure upon circulation have been reviewed and further investigated employing dogs.<sup>30</sup> The operations were carried out in three stages at intervals of several weeks. A decline of blood pressure averaging 38 mm. Hg occurred. Restoration began within a few weeks of the last stage of the sympathectomy and reached the preoperative level in an average time of six months. Blood volume and blood viscosity were not appreciably altered. Cardiac output was reduced during the stage of hypotension and also late after restoration of the blood pressure to normal values. Varying amounts of adrenalin given before and several weeks to one or two years after the sympathetic ganglionectomy produced essentially similar blood pressure responses. Blood pressure lowering seems more prolonged and adrenalin hyperresponsiveness less evident in these experiments than in those involving cord destruction.

These studies on vascular tone during perfusion of isolated organs, stimulation of carotid sinus and depressor nerves, destruction of the spinal cord, and excision of the paravertebral sympathetic chains and ganglia seem to



indicate that denervated blood vessels are capable of developing an intrinsic tone. This tone is not dependent upon nerve regeneration during the first several weeks and may occur at times under conditions that would exclude an adrenalin "sensitization" factor. Cannon<sup>9</sup> stated: "Until definite proof that an external agent operates to restore 'tone' in denervated vascular muscle I believe we are warranted in assuming that the restoration results from an intrinsic property of the muscle itself." This property of denervated smooth muscle probably presents the major limitation to the effectiveness of clinical sympathetic nerve surgery for vascular disease.

#### GENERAL LIMITATIONS OF SYMPATHECTOMY

*The Role of Sympathetic Vasodilator Pathways.*—There are influences in addition to the three just discussed that limit or qualify the effect of regional and extensive sympathetic denervation of the peripheral vascular bed. Operations evidently do not uniformly alter circulation through the body. A difference exists between the effect upon circulation of regional and of extensive sympathectomies. Herrick, Essex, and Baldes<sup>67</sup> and Schneider<sup>68</sup> believed from evidence obtained after lumbar sympathetic ganglionectomy of the hind leg of the dog that increased circulation may remain double the control values as long as twenty-four to thirty-four months. Sympathectomies of normal legs of patients incidentally effected by operation for megacolon produce an elevation of skin temperature that may persist many years. Essex, Herrick, Baldes, and Mann<sup>69</sup> determined that nine and ten years after lumbar ganglionectomy of one hind leg in a dog the blood flow returned to almost the same as that of the normal limb. Sympathectomies of the entire body of the dog<sup>30</sup> effect a less conspicuous change in circulation. Blood volume and viscosity are not appreciably altered and cardiac rate and output are decreased. Sympathectomies of most of the body of patients with hypertension<sup>2, 70</sup> have not altered venous pressure or arm-to-tongue circulation time and have slightly decreased the basal heart rate and cardiac output. Extensive or total sympathectomy does not double the rate of circulation of blood through the body as regional sympathectomy may for the leg.

This difference between the effect of regional and of total sympathectomy may be related in part to the role played by the vasodilator mechanism of the body. The effect of a sympathectomy upon each organ or body structure will vary with the relative importance of vasoconstrictor influence or tone in the regulation of its circulation. Sympathetic nerves may carry vasodilator fibers and the effect of sympathectomy will vary with the number and importance of the vasodilator fibers divided.

A complex vasodilator system exists in some animals and also in man. McDowall<sup>7</sup> and Burn<sup>71</sup> have recently summarized the current opinions related to this system. Nervous vasodilator mechanisms are in part extrasympathetic. They are related locally to Lovén reflexes, axon reflexes, and antidromic impulses. They are related centrally to vasodilator impulses that travel from centers in the medulla and spinal cord through specialized nerves such as the

chorda tympani and nervus erigens and according to some evidence through the posterior nerve roots along many sensory nerves.

Nervous vasodilator fibers are also in part contained in the sympathetic nervous system. Activity varies in different parts of the body. Burn<sup>71</sup> stated that sympathetic vasodilatation is easily demonstrable in the muscles of the dog, detectable in the intestines, and absent in the skin except for that of the ear. He also stated that there are important differences in different species. The rabbit and monkey have no demonstrable sympathetic vasodilators to muscle, the rat has a few, and the dog and the hare many.

Rosenbleuth and Cannon<sup>72</sup> suggested that the vasodilator system consists of autonomic dilators primarily distributed to skeletal muscle, parasympathetic dilators such as the chorda tympani and nervi erigentes, and dorsal root dilators, distributed primarily to the skin and viscera. Sewall and Sanford<sup>73</sup> early recorded the finger volume of patients and found that weak stimulation of the ulnar nerve produced dilatation and stronger stimulation constriction by reflexes activated by stimulation of sensory filaments.

Detailed evidence of the presence or the significance of sympathetic vasodilator fibers to various parts of the body in man cannot be easily obtained. Lewis and Pickering<sup>74</sup> reported evidence for the presence of sympathetic vasodilators to the fingers. This evidence was obtained by heating the body of patients and observing the color response of a cool extremity. Until further study demonstrates the presence and distribution or the absence of sympathetic vasodilators in man a possible relationship to the current surgical treatment of vascular disease must receive consideration.

A sympathectomy in a patient might interrupt vasodilator pathways to such important structures as muscle. It might interrupt the afferent sensory fibers from the viscera that travel in the sympathetic nerves and have been described in dogs by Moore and Singleton.<sup>75</sup> It might also interrupt autonomic proprioceptive fibers from smooth muscle (Langworthy<sup>12</sup>). Interruption of afferent pathways could alter extrasympathetic as well as sympathetic vasodilator reflexes. Splanchnicectomy might also interfere with the vasodilatation of the intestines produced by small doses of adrenalin, as has been reported in acute experiments in the dog and cat by Hartman and Fraser.<sup>76</sup> While lumbar sympathectomy alone in acute experiments did not abolish the vasodilating action of small doses of adrenalin, Wierzuchowski,<sup>77</sup> and Hartman and Fraser<sup>76</sup> did observe that complete denervation, both sympathetic and somatic, abolished this action of adrenalin in perfused hind legs of the dog. Similarly, Wierzuchowski<sup>77</sup> observed that there was no vasodilatation from adrenalin in isolated and perfused hind legs of frogs, or in similarly treated rabbits' ears and heads. There was also no reversal of the action of F 933 under these conditions. It would, therefore, seem that adrenalin vasodilatation would be influenced by sympathectomy more in the splanchnic or visceral area than in extremities.

Postural hypotension is evident in man after extensive sympathectomies. Exercise in extensively or completely sympathectomized patients, dogs, and

cats causes a lowering rather than an elevation of blood pressure. Until more information related to the subject is available, the possibility exists that extensive sympathectomies in man may alter vasodilator mechanisms as well as interrupt vasoconstrictor pathways.

The functional balance between sympathetic vasoconstrictors and sympathetic vasodilators and the functional effect of sympathectomy upon circulation evidently differs from organ to organ and structure to structure. McDowall<sup>7</sup> has reviewed the detailed experiments that indicate that sympathetic vasoconstrictors extend to almost every organ and structure of the body but that vasodilators are preponderantly evident to some. Heymans, Bouckaert, and Regniers<sup>78</sup> have reviewed the complex role played by the modulator nerves of the carotid sinus and the heart and the aorta. These nerves act through the vasomotor centers to control the balance between vasoconstrictors and vasodilators. The old principle that excitement, sham rage, and hemorrhage may contract the vessels of the skin, the spleen, and the splanchnic region and at the same time assure adequate circulation through the vessels of the heart, brain, and muscles is to an important degree dependent upon this balance. Sympathectomy would increase circulation least in those organs that receive a preponderant vasodilator influence.

*The Function of Arteriovenous Anastomoses.*—Certain organs have a shunt mechanism that further complicates the effect of sympathectomy. These shunts are especially evident in the skin where they aid the regulation of body heat. They conduct blood directly from fine arteries to fine veins, and are called arteriovenous anastomoses. The development of our understanding of the importance of these direct communications has been well reviewed by Clark.<sup>79</sup> Arteriovenous anastomoses are known to exist in man in the penis, fingers, and toes, and probably have a wider distribution as they are known to have in animals. The occurrence of painful glomus tumors in patients demonstrates both their presence and their rich nerve supply.

Anastomoses in the rabbit's ear constrict with adrenalin and faradic stimulation of sympathetic nerves and dilate after histamine and acetylcholine. When widely open they may conduct oxygenated arterial blood directly into veins at the expense of the capillary circulation. Their general behavior is similar to the activity of small arteries and arterioles although irregular periodic contractions are more active and less dependent upon changes of the general circulation. A sympathectomy to an area, should it open widely these shunts, might effect an increase of circulation through these multiple arteriovenous fistulas without increasing the supply of blood to the tissues through the capillaries.

*Humoral and Metabolic Control of Circulation Through Denervated Vessels.*—Release of central vasomotor tone by sympathectomy does not protect the vascular bed from responding to many humoral influences. Adrenalin may be liberated by the adrenal glands of most patients after regional head, arm, or leg sympathectomies during exercise, nervous strain, and exposure and may have an enhanced reaction upon the denervated vascular bed. Sympathin will

experimentally accelerate a denervated heart (Newton, Zwemer, and Cannon<sup>80</sup>) and elevate blood pressure (Cannon and Bacq<sup>81</sup>). Therefore, if sympathin is clinically significant it may have an action on denervated blood vessels similar to that of adrenalin.

Following an accurate splanchnicectomy the denervated adrenals should not secrete unless or until regeneration occurs. Stewart and Rogoff<sup>82</sup> demonstrated that denervation of the adrenal glands of cats arrested the spontaneous liberation of adrenalin that they believe occurs, and also the liberation affected by nerve stimulation. Sympathin production may also be cut down as sympathetic denervation of patients is extended to the subtotal or total sympathectomy. The more extensive sympathectomies currently employed for hypertension should therefore be less limited by adrenalin-like hormones.

Another humoral agent, angiotonin (Page and Helmer<sup>83</sup>), or hypertensin (Munoz, Braun-Menendez, Fasciolo, and Leloir<sup>84</sup>), may occur in hypertension. It is associated with an alteration of renal circulation and metabolism. This agent may act directly upon blood vessels deprived of their sympathetic nerve supply even after complete experimental sympathectomy (Heymans, Bouckaert, Elaut, Bayless, and Samaan,<sup>85</sup> Freeman and Page,<sup>86</sup> Alpert, Alving, and Grimson,<sup>87</sup> Verney and Vogt<sup>88</sup>). Principles from the pituitary and the adrenal cortex seem to influence the capillaries more than the smaller arteries or arterioles.

Experiments dealing with blood flow and blood vessel dilatation in muscles during rest and activity, experiments dealing with reactive hyperemia, and those dealing with warming and cooling of smooth muscle all indicate that tissue metabolism and metabolic products may influence the peripheral vascular bed. Dale<sup>89</sup> has reviewed the pharmacology of histamine and its action on capillaries and small vessels and that of acetylcholine and its action on arterioles and small arteries, and that of other substances originating peripherally and acting upon the vascular bed. Cannon<sup>9</sup> discussed the possible influence upon blood vessels of lactic acid, carbon dioxide, lack of oxygen, histamine, acetylcholine, and many products of metabolism and concluded: "We have no decisive evidence regarding the agencies which adapt the tone of the blood vessels to the needs of organs as they vary between rest and activity."

Temperature may profoundly influence blood flow and metabolism in sympathectomized limbs (Freeman<sup>90</sup> and Freeman and Zeller<sup>91</sup>). These authors have shown that coldness of the hands or feet of patients with certain vascular disorders may markedly effect local metabolic control of blood vessels. Infection may warm up previously cool extremities and locally improve circulation. The normal skin temperature gradient with the hands and feet usually several degrees cooler than the body must have some metabolic influence upon the blood vessels and might influence the development of certain peripheral vascular diseases.

*Further Limitations of Preganglionic Sympathectomy.*—Decentralization of the stellate or the lower lumbar sympathetic ganglia for peripheral vascular disease is at present currently popular. There are, however, limitations to this procedure in addition to the increased likelihood of nerve regeneration.

It has been assumed that all synapses between pre- and postganglionic fibers supplying the arm are located in the stellate and second thoracic ganglia, and those supplying the leg in the third and fourth lumbar and sacral ganglia. Preganglionic fibers to the arm travel through the anterior spinal roots from the third, fourth, or fifth thoracic segments to about the ninth. Fibers to the leg travel from the lower one, two, or three thoracic segments to and through the third lumbar. It is possible that as these preganglionic fibers pass through the sympathetic chain toward the upper thoracic or the lower lumbar and sacral ganglia some may form synapses with cells that then send postganglionic fibers to the limbs. Surgical division of the thoracic chain between the second and third dorsal or the lumbar chain just above the third lumbar vertebra would then be a postganglionic sympathectomy for such fibers. Experiments determining the presence or absence of synapses between pre- and postganglionic fibers central to the site of the usual "preganglionic" sympathectomies have not been reported. Evidence of pathways other than those usually recognized has been obtained in patients (Foerster<sup>92</sup>) and in dogs (Derom and Grimson<sup>93</sup>). This evidence indicates that some sympathetic vasoconstrictor fibers entering the midthoracic sympathetic chain may reach the cervical ganglia before returning through the stellate ganglia to the arm. Livingston<sup>94</sup> and Sheehan<sup>11</sup> discussed the possible role of postganglionic cells, located proximal to the operative field of an arm or leg ganglionectomy, in late nerve regeneration. The so-called preganglionic sympathectomies may then be also postganglionic sympathectomies for an undetermined number of sympathetic fibers. The preganglionic sympathectomy is also postganglionic for those postganglionic cell bodies that are destroyed by ischemia or fibroses after transplantation or encapsulation performed to diminish regeneration.

Although isolated or decentralized sympathetic ganglia lose by degeneration the postganglionic fibers passing through them, they remain as a group of relatively intact postganglionic cells. These cell stations would maintain their postganglionic connection with blood vessels and might be capable of influencing vascular tone by automatic activity, or by stimulation by reflex or humoral influences.

Sternschein<sup>95</sup> reviewed the early evidence indicating that a decentralized sympathetic ganglion may exert a tonic influence through its postganglionic fibers. From experiments upon the relationship between the cervical ganglia and the pupil of the rabbit and the cat he concluded that the superior cervical ganglion augments or increases the central dilator tonus that it transmits from the central nervous system and also suppresses dilator tonus of peripheral or humoral origin. Boshamer<sup>96</sup> concluded from experiments in the frog that sympathetic ganglia disconnected from the spinal cord assist the new tone of blood vessels. He suggested that this phenomena might explain the difference between pre- and postganglionic sympathectomies observed by Meltzer and Auer.<sup>39</sup> Hermann and Guiran<sup>97</sup> reviewed and further amplified the experiments with frogs indicating vasoconstrictor tonus originating in sympathetic ganglia. Heymans and Brouha<sup>6</sup> reviewed later evidence for and against the assumption that decentralized sympathetic ganglia might exert a tonic influ-

ence through their postganglionic fibers and concluded that they do effect some control. Emphasis has been placed upon the observations of Govaerts and Bremer<sup>68</sup> that the decentralized superior cervical ganglion of a cat develops a tonic influence upon heart rate after several days and that action currents reappear in the postganglionic cardiac nerves.

Evidence that decentralized ganglia may exert an influence upon blood pressure may also be obtained by comparing the results of experiments employing low cervical cord section, cord destruction, and total sympathectomy in dogs. Physiologists have long recognized that low cervical cord section lowers blood pressure to around 50 to 80 mm. of mercury, but that a recovery toward normal values occurs within twenty-four hours. Also, the cord destruction experiments described previously<sup>64, 65</sup> indicate a similar immediate lowering of pressure and a return to normal within one day or two. In these two types of experiments the sympathetic ganglia and their postganglionic fibers remain intact. The effect upon blood pressure of removal of the ganglia of the paravertebral sympathetic chains, "total sympathectomy," is however somewhat different. I have, in unpublished experiments, combined the two transthoracic and the transabdominal sympathectomies of total sympathectomy in dogs into one operation. Four survived two to seven days. Blood pressures were maintained between 40 and 86 mm. Hg. These values compare favorably with values observed in dogs immediately after cord section or cord destruction. Removal of the paravertebral chains and ganglia for chronic physiologic experiments is usually accomplished by employing three consecutive operations at intervals of several weeks.<sup>30</sup> A lowering of blood pressure occurs only after the second or third operation. Restoration begins within a few weeks of the last operation and reaches the preoperative level in an average time of six months. It is thus evident that while the presence of an intact paravertebral sympathetic chain, with its ganglia and postganglionic connections, facilitates prompt restoration of near normal blood pressure values and of peripheral resistance of the body as a whole, the absence of the paravertebral ganglia delays recovery until sympathetic nerve regeneration may occur.

The exact nature of the influence exerted by decentralized sympathetic ganglia upon the vascular bed has not been demonstrated but may be discussed. Hermann, Morin, and Vial<sup>66</sup> stated that they are inclined to believe that the sympathetic ganglia manage extramedullary vasomotor tone but they stated that their opinion concerning the action of the ganglia is not certain. Origin in sympathetic ganglia of automatic activity has little physiologic basis and is not currently accepted. I believe, however, that the experiments related here may be explained by the assumption that sympathetic ganglia are capable of modifying vascular tone by reflex activation from stimuli that it may receive from the vascular bed. Langworthy<sup>12</sup> has presented evidence that the entire autonomic system, sympathetic and parasympathetic alike, is influenced to an important degree by stimuli received from smooth muscle. He stated: "The autonomic system has been considered as purely a motor system, composed of pre-ganglionic and postganglionic neurons. However, it is influenced by sensory

impulses originating in the smooth muscle and glandular tissues, so that it operates on the basis of segmental reflex arcs. The normal function of smooth muscle is dependent on proprioceptive stimuli from the muscle itself. The autonomic fibers are also subject to control from all levels of the central nervous system, including the motor cortex."

Decentralized sympathetic ganglia may also be stimulated directly by humoral agents. This would influence the tone of the vascular bed supplied by its postganglionic fibers. Cannon and Rosenbleuth<sup>99</sup> have demonstrated that acetylcholine has a much greater effect in stimulating the superior cervical sympathetic ganglion chronically deprived of its preganglionic innervation than the superior cervical ganglion acutely denervated. Burn<sup>100</sup> has reviewed the relation of adrenalin to acetylcholine in the nervous system and the relation of both to the function of sympathetic ganglia.

*Abnormal Spasm of the Peripheral Vascular Bed.*—Many of the limitations of sympathectomy discussed here have related to the circumstances encountered in relatively normal blood vessels. The occurrence of abnormal local spasm of the vascular bed in Raynaud's disease has interested surgeons since the report of Adson and Brown<sup>55</sup> that sympathectomy afforded relief. Lewis<sup>101</sup> observed the development of skin discoloration associated with local cooling, and the effect of local heating of the hands of patients with Raynaud's disease. He demonstrated that the spasm may occur as a local fault not related to abnormal vasoconstrictor tone. Postganglionic sympathectomy effected by blocking the ulnar nerve with nococain improved discoloration already present only partially and partially retarded the subsequent development of local blood vessel spasm. Occurrence of some degree of spasm in patients after pre- or postganglionic sympathetic denervation is a common observation. Sympathectomy in this form of vasospastic disease is then limited both by mechanisms controlling the normal vascular bed and by a superimposed local abnormality of the blood vessels.

#### CLINICAL INTERPRETATION

Partial or complete excision or decentralization of the ganglionated paravertebral sympathetic chain may effect varying degrees of relaxation of the smooth muscle of blood vessels and some increase of circulation. It does not effect complete relaxation of blood vessels or great increase of blood flow. The vasomotor fibers of the sympathetic nervous system are largely the efferent pathways of a complex proprioceptive mechanism that regulates or modulates the peripheral resistance but is not responsible for its maintenance. The therapeutic effect of interruption of these efferent sympathetic pathways for disease is limited by the factors just reviewed that are responsible for the maintenance in denervated blood vessels of tone and control. The most important of these factors is the inherent ability of smooth muscle to maintain an independent tone. Another important factor is the ability of these muscles to respond to humoral substances such as adrenalin, acetylcholine, and angiotonin, or hypertensin, to products of tissue metabolism such as lactic acid.

carbon dioxide, and histamine, and to changes of temperature. Blood vessels may be to some extent under extra sympathetic nervous control or, if the denervation be preganglionic, under reflex or other restraining control through the isolated ganglia. Late after sympathectomy, preganglionic nerve regeneration through isolated ganglia or postganglionic nerve regeneration from cells central to the operative defect may occur.

Regardless of these and the other limiting factors that have been reviewed, temporary or permanent interruption of the sympathetic pathways accomplishes certain therapeutic benefits for patients with many disease processes. The greatest benefits are achieved in disease processes associated with a disturbance of the proprioceptive regulatory function of the sympathetic nervous system. An example of the encouraging results that may be obtained in patients with a central disturbance of the reflex proprioceptive mechanism is afforded by the effectiveness of sympathectomy in patients with a neurogenic variety of hypertension.<sup>102</sup> An example of the results in patients with a peripheral disturbance of the reflex proprioceptive regulation is afforded by the effectiveness of sympathetic block in relieving the spasm of collateral vessels that develops after extensive vascular injury or arterial embolism. There are, however, not many disease processes that can originate as abnormal central or reflex sympathetic vasoconstriction.

Sympathectomy may also benefit patients with conditions such as Raynaud's disease, scleroderma, thromboangiitis obliterans, and arteriosclerotic vascular occlusion that evidently are not initiated by excess sympathetic tone. Benefits in patients with these conditions may be largely related to increase of the temperature of the extremity, to a slight improvement of circulation, and to elimination by the sympathectomy of the constant fluctuations of tone that are ordinarily induced by the vasomotor nerves. It is common observation that treatment of peripheral vascular diseases by sympathectomy is more satisfactory in the legs than in the arms. There seems to be evidence that the legs, because of their dependent position, are more actively influenced by sympathetic vasomotor tone of proprioceptive origin. Sympathectomy may then effect its greater benefit to the legs by interrupting this tone and also by introducing, during changes of posture, an uncompensated passive vascular exercise.

Surgeons have not agreed upon the form of sympathectomy that should be employed for peripheral vascular disease of the extremities. It seems to me that the sympathectomy should be a radical ganglionectomy to minimize nerve regeneration and to eliminate any buffering or reflex control that might be afforded by decentralized ganglia. It also seems that the "adrenalin sensitization" phenomenon, upon which the preganglionic type of sympathectomy is based, is not sufficiently important clinically to warrant risking regeneration. Both a ganglionectomy and a preganglionic sympathectomy "sensitize" blood vessels to adrenalin. I employ preganglionic sympathectomy only in instances of disease of one arm since a unilateral Horner's syndrome may be objectionable.

Special problems have become important clinically as sympathectomy has been extended for the treatment of hypertension to include part or all of the trunk and the viscera as well as the extremities. These have been reviewed.



It seems important that there are sympathetic vasodilator pathways to muscle and to many of the viscera. Circulation through organs preponderantly supplied by vasodilators will not be improved as much as it will in those preponderantly supplied by vasoconstrictors. Clinical studies have demonstrated that although the circulation of an extremity alone may be increased by regional sympathectomy, the over-all circulation of the entire body after subtotal to total sympathectomy is, as evidenced by the cardiac output, somewhat decreased.

Clinical experience with the treatment of hypertension seems to indicate that elimination of abnormal reflex vasoconstrictor tone of central origin more effectively reduces blood pressure as sympathectomy of the body is made more and more complete. The splanchnic area, including the kidneys and the adrenal glands, does not seem to be more important than other large vascular areas of the body.<sup>30, 103</sup> Extensive sympathectomy also interferes with normal reflex adjustments of vasoconstrictor tone that occur with changes of position of the body. Difficulties with postural hypotension seem to be greater when denervation is directed toward the dependent half of the body, as it is in the techniques used for splanchnicectomy, than when it is directed toward the upper three-quarters or all of the body as it is with the subtotal to total paravertebral sympathectomy.

The physiologic and anatomic changes effected by regional or extensive sympathectomy are complex. Experimental investigation has contributed valuable information but has not solved all of the problems. The surgeon still has difficulty determining the indications for and the results of various procedures. The value of the novocain block as a prognostic procedure is questionable since it effects an acute change of circulation and does not represent the conditions that will maintain several days, months, or years, after a sympathectomy. It does not indicate the long-term influence upon a chronic peripheral vascular disease process that may result from elimination by sympathectomy of central proprioceptive influences. Similarly evaluation of the late result of a sympathectomy may be difficult and easily misjudged because of enthusiasm. Fortunately, sympathectomy is a relatively safe surgical procedure if detailed general examination of the patient demonstrates no contra-indication. It remains a valuable adjunct to the conservative treatment of peripheral vascular disease.

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## Book Reviews

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**Neuro-Ophthalmology.** By Donald J. Lyle, B.S., M.D., Department of Anatomy, Medical College, University of Cincinnati, Cincinnati, Ohio. Ed. 1. Pp. 395, with 234 illustrations. Springfield, Ill., 1945, Charles C Thomas, Publisher. \$10.50.

This book according to the preface is written to bring together, in brief but comprehensive and coordinated manner, those many phases of neurology, in so far as they concern, directly or indirectly, neuro-ophthalmology.

The result is another textbook of neurology with special reference to ophthalmology. It is tedious reading, perhaps due to its brevity. As a reference book it should be very useful to the ophthalmologist who is untrained in neurology.

The following paragraph, p. 81, gives one the impression that the author is writing about a subject with which he has not had a wide experience.

"The ophthalmic division is most frequently involved in trigeminal neuralgia. The supra-orbital branch is particularly affected. ----- The ophthalmic or first division is less frequently involved by tic douloureux than either the second or third. The third is most commonly affected."

An extensive bibliography of 1718 references grouped alphabetically is listed at the end of the book, some of which are referred to by numbers in the text, but many are not.

The 234 illustrations are all well reproduced.

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### Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers and as space permits.

**TEXTBOOK OF ANESTHETICS.** By R. J. Minnitt, M.D., D.A., and John Gillies, M.C., M.B., Ch.B., D.A., Royal Infirmary, Edinburgh, Scotland. Cloth. Price \$7. Pp. 487, with 199 illustrations. Baltimore, 1944, Williams & Wilkins Company.

**PYE'S SURGICAL HANDICRAFT.** Edited by Hamilton Bailey, F.R.C.S., England. Cloth. Price \$8. Pp. 628, with 724 illustrations. Baltimore, 1944, Williams & Wilkins Company.

**POET PHYSICIANS (An Anthology of Medical Poetry Written by Physicians).** Compiled by Mary Lou McDonough. Cloth. Price \$5. Pp. 204. Springfield, Ill., 1945, Charles C Thomas, Publisher.

**PERIPHERAL NERVE INJURIES: PRINCIPLES OF DIAGNOSIS.** By Captain Webb Haymaker, M.C., A.U.S., Army Institute of Pathology, Washington, D. C., and Major Barnes Woodhall, M.C., A.U.S., Chief Neurology Section, Walter Reed Hospital, Washington, D. C. Cloth. Pp. 227, with 225 illustrations. Philadelphia and London, 1945, W. B. Saunders Company.

**MODERN METHODS OF AMPUTATION.** By Edmundo Yasconcelos, Professor, University of Sao Paulo. Introductory Survey by Major General Norman T. Kirk. Cloth. Price \$10. Pp. 253, with 258 illustrations. New York, 1945, Philosophical Library, Inc.

**DUODENAL AND JEJUNAL PEPTIC ULCER.** By Rudolf Nissen, M.D., Attending Surgeon, Jewish Hospital of Brooklyn. Cloth. Pp. 143. New York, 1945, Grune & Stratton, Inc.

**RADIOLOGIC EXAMINATION OF THE SMALL INTESTINE.** By Russ Golden, M.D., Professor of Radiology, College of Physicians and Surgeons, Columbia University. Cloth. Price \$6. Pp. 239, with 75 illustrations. Philadelphia, 1945, J. B. Lippincott Company.

**CLINICAL ROENTGENOLOGY OF THE DIGESTIVE TRACT.** By Maurice Feldman, M.D., Assistant Professor, Gastroenterology, University of Maryland. Cloth. Price \$7. Pp. 769. Baltimore, 1945, Williams & Wilkins Company.

**PENICILLIN THERAPY INCLUDING TYROTHRICIN AND OTHER ANTI-BIOTIC THERAPY.** By John A. Kolmer, M.S., M.D., Dr. Ph., Sc.D., LL.D., L.H.D., F.A.C.P., Professor of Medicine in the School of Medicine and School of Dentistry, Temple University. Cloth. Pp. 302. New York, 1945, D. Appleton-Century Company, Inc.

**NEURO-OPHTHALMOLOGY.** By Donald J. Lyle, B.S., M.D., Department of Anatomy, Medical College of the University of Cincinnati. Cloth. Price \$10.50. Pp. 395, with 234 illustrations. Springfield, Ill., 1945, Charles C Thomas, Publisher.

**DISEASES OF THE NERVOUS SYSTEM IN INFANCY, CHILDHOOD AND ADOLESCENCE.** By Frank R. Ford, M.D., Associate Professor of Neurology, The Johns Hopkins University. Cloth. Pp. 1,143, with 164 illustrations. Springfield, Ill., 1944, Charles C Thomas, Publisher.

**ESSENTIALS OF BODY MECHANICS IN HEALTH AND DISEASE.** By J. T. Goldthwait, M.D., F.A.C.S., LL.D., L. T. Brown, M.D., F.A.C.S., L. T. Swaim, M.D., John G. Kuhns, M.D., F.A.C.S., and Wm. J. Kerr, M.D., F.A.C.P. Cloth. Price \$5. Pp. 337, with 128 illustrations. Philadelphia, 1945, J. B. Lippincott Company.

**MODERN MEDICINE ANNUAL 1944.** Abstracted Articles of Various Authors. Cloth. Pp. 853. Minneapolis, 1945, Modern Medicine Publishing Company.

**CLINICAL TRAUMATIC SURGERY.** By John J. Moorhead, B.S., M.D., D.Sc., F.A.C.S. (D.S.M.), Columbia University. Cloth. Pp. 747, with 500 illustrations. Philadelphia, 1945, W. B. Saunders Company.

**A MANUAL OF SURGICAL ANATOMY.** By Tom Jones and W. C. Shepard, Office of the Surgeon General, National Research Council, Washington, D. C. Cloth. Pp. 195, with 139 illustrations. Philadelphia, 1945, W. B. Saunders Company.

**BONE GRAFTING IN THE TREATMENT OF FRACTURES.** By J. R. Armstrong, M.D., M.Ch., F.R.C.S., Orthopaedic Department with Fracture Clinic, Charing Cross Hospital, London. Cloth. Price \$7. Pp. 175, with 204 illustrations. Baltimore, 1945, Williams & Wilkins Company.

**RYPIN'S MEDICAL LICENSURE EXAMINATIONS.** By Harold Rypins, M.D., Edited by Walter L. Bierring, M.D., National Board of Medical Examiners. Cloth. Price \$6. Pp. 545. Philadelphia, 1945, J. B. Lippincott Company.

**THE YEAR BOOK OF GENERAL SURGERY 1944.** Edited by Evarts A. Graham, A.B., M.D., Washington University School of Medicine, St. Louis, Mo. Cloth. Price \$3.00. Pp. 736, with 271 illustrations. Chicago, 1944, The Year Book Publishers, Inc.

**THE URINARY TRACT, A HANDBOOK OF ROENTGEN DIAGNOSIS.** By H. Dabney Kerr, M.D., and Carl L. Gillies, M.D., Iowa City. Cloth. Price \$5.50. Pp. 320, with 475 illustrations. Chicago, 1944, The Year Book Publishers, Inc.

**FRACTURES OF THE JAWS.** By Robert H. Ivy, M.D., D.D.S., F.A.C.S., and Lawrence Curtis, A.B., M.D., D.D.S., F.A.C.S., University of Pennsylvania. Cloth. Price \$4.50. Pp. 174, with 199 illustrations. Philadelphia, 1945, Lea & Febiger.

**NITROUS OXIDE-OXYGEN ANESTHESIA.** By Major F. W. Clement, M.D., M.C., A.M.S. Cloth. Price \$4.50. Pp. 288, with 92 illustrations. Philadelphia, 1945, Lea & Febiger.

**THE INTERVERTEBRAL DISC.** By F. Keith Bradford, M.D., Houston, and R. Glen Spurling, M.D., Louisville. Cloth. Price \$4.00. Pp. 192, with 70 illustrations. Springfield, Ill., 1945, Charles C Thomas, Publisher.

**PEDIATRICS X-RAY DIAGNOSIS.** By John Caffey, A.B., M.D., New York. Cloth. Price \$12.50. Pp. 838, with 711 illustrations. Chicago, 1945, The Year Book Publishers, Inc.

**A TEXTBOOK OF SURGERY.** By John Homans, M.D., Clinical Professor of Surgery, Emeritus. Cloth. Price \$8.00. Pp. 1,278, with 530 illustrations. Springfield, Ill., 1945. Charles C Thomas, Publisher.

**TEXTBOOK OF OBSTETRICS.** By Henricus J. Stander, M.D., F.A.C.S., Professor of Obstetrics and Gynecology, Cornell University Medical College. Cloth. Pp. 1,277, with 740 illustrations. New York, 1945, D. Appleton-Century Company, Inc.

**A TEXTBOOK OF NEURO-ANATOMY.** By Albert Kuntz, Ph.D., M.D., Professor of Micro-Anatomy, St. Louis University School of Medicine. Cloth. Price \$6.50. Pp. 478, with 328 illustrations. Philadelphia, 1945, Lea & Febiger.

**A HANDBOOK OF ROENTGEN DIAGNOSIS, THE OSSEOUS SYSTEM.** By Vincent W. Archer, M.D., Professor of Roentgenology, University of Virginia Department of Medicine. Cloth. Price \$5.50. Pp. 320, with 148 illustrations. Chicago, 1945, The Year Book Publishers, Inc.

**CLASSIC DESCRIPTIONS OF DISEASE.** By Ralph H. Major, M.D., Professor of Medicine, University of Kansas School of Medicine. Cloth. Price \$6.50. Pp. 679, with 158 illustrations. Springfield, Ill., 1945, Charles C Thomas, Publisher.

**HEY GROVES' SYNOPSIS OF SURGERY.** Edited by Cecil P. G. Wakely, C.B., D.Sc., Senior Surgeon, King's College Hospital. Cloth. Price \$6.00. Pp. 632, with 195 illustrations. Baltimore, 1945, Williams & Wilkins Company.

**A HANDBOOK FOR DISSECTORS.** By J. C. Boileau Grant, M.D., Professor of Anatomy, University of Toronto, and H. A. Cates, Associate Professor of Anatomy, University of Toronto. Cloth. Price \$3.50. Pp. 390, with 10 illustrations. Baltimore, 1945, Williams & Wilkins Company.

**FRACTURES AND ORTHOPAEDIC SURGERY FOR NURSES AND MASSEUSES.** By Arthur Naylor, Ch.M., M.D., Res. Surg. Officer, Westwood E.M.S. Hospital. Cloth. Price \$5.00. Pp. 288, with 243 illustrations. Baltimore, 1945, Williams & Wilkins Company.



**ACUTE INJURIES OF THE HEAD, THEIR DIAGNOSIS, TREATMENT COMPLICATIONS AND SEQUELS.** By G. F. Rowbotham, B.Sc., Surgeon in Charge, Department of Neurological Surgery, Newcastle General Hospital. Cloth. Price \$8.50. Pp. 424, with 201 illustrations. Baltimore, 1945, Williams & Wilkins Company.

**VARICOSE VEINS OF THE LOWER EXTREMITIES (Monograph).** By Anthony M. Barone, M.D., 4000 West North Avenue, Chicago, Ill. Paper. Pp. 51, with 10 illustrations.

**PHYSICAL CHEMISTRY OF CELLS AND TISSUES.** By Rudolf Hüber, M.D., Department of Physiology, University of Pennsylvania. Cloth. Price \$9.00. Pp. 676, with 70 illustrations. Philadelphia, 1945, The Blakiston Company.

**GENERAL AND PLASTIC SURGERY.** By J. Eastman Sheehan, M.D., Professor of Plastic Reparative Surgery, New York Polyclinic Medical School and Hospital. Cloth. Price \$6.75. Pp. 345, with 495 illustrations. New York, 1945, Paul B. Hoeber, Inc.

**THE MARCH OF MEDICINE.** By the New York Academy of Medicine, Lectures to the Laity, composed of Charles D. Ryan, M.D., Frank Fremont Smith, M.D., Philip Potter, M.D., Alexander T. Martin, M.D., George F. Cahill, M.D., George T. Ward, M.D., and Wilson G. Smillie, M.D. Cloth. Price \$1.75. Pp. 121. New York, 1945, Columbia University Press.

**AMPUTATION PROSTHESIS.** By Atha Thomas, M.D., F.A.C.S., Associate Professor of Surgery (Orthopedics), University of Colorado School of Medicine, and Chester C. Haddan, President of the Association of Limb Manufacturers of America. Cloth. Price \$8.00. Pp. 305, with 207 illustrations. Philadelphia, 1945, J. B. Lippincott Company.

**MODERN UROLOGY FOR NURSES.** By Sheila Maureen Dwyer, R.N., B.S., Director of Nursing, Southampton Hospital, Southampton, New York, and George W. Fish, M.D., Associate Professor of Urology, College of Physicians and Surgeons, Columbia University, New York. Cloth. Price \$3.25. Pp. 287, with 66 illustrations. Philadelphia, 1945, Lea & Febiger.

**PATHOLOGY IN SURGERY.** By N. Chandler Foot, M.D., Professor of Surgical Pathology, Cornell University Medical College, Surgical Pathologist, New York Hospital. Cloth. Pp. 489, with 368 illustrations. Philadelphia, 1945, J. B. Lippincott Company.

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## Announcement

### Urology Award

The American Urological Association offers an annual award "not to exceed \$500" for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the Committee on Scientific Research deems none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the secretary, for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming meeting of the American Urological Association, to be held at the Netherland Plaza, Cincinnati, Ohio, July 22 to 25, 1946.

Essays must be in the hands of the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tenn., on or before July 1, 1946.

# SURGERY

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## Original Communications

### PREOPERATIVE DIETARY MANAGEMENT FOR SURGICAL PATIENTS

WITH SPECIAL REFERENCE TO LESIONS OF THE STOMACH AND DUODENUM

RICHARD L. VARCO, M.D., MINNEAPOLIS, MINN.

*(From the Department of Surgery, University of Minnesota Medical School)*

#### FOREWORD AND INTRODUCTION

IN THE past a surgeon matured by focusing his attention upon, and acquiring a broad familiarity with, pathologic tissues and a facility with operative techniques. Such achievements appeared paramount because so many technical developments in surgery antedated a commensurate knowledge of physiologic processes, or application of this knowledge, when it was present. A transition is being effected. One of the most laudable changes in recent decades has been the steady reduction in the number of "emergency operations." The emphasis on speed and manual dexterity has been supplanted by a more leisurely technique stressing precision and a genuine respect for tissues that yields generous dividends in improved wound healing and decreased post-operative reaction. In addition, the surgical viewpoint is being altered by a shift in emphasis during the years of graduate training from a background of anatomy and pathology exclusively to one including an orientation in the biologic sciences. Merely fortuitous circumstances have not brought about this transition, but it has resulted rather from the wise guidance of those teachers recognizing the advantages ultimately so accruing to the earnest student of surgery. A broad knowledge of fundamental physiologic processes enhances the capacity for recognition of pathologic deviations, frequently arouses a curiosity as to the mechanisms involved, and often suggests appropriate therapeutic principles. Maintenance of this familiarity with the biologic sciences and their application to phenomena encountered in clinical material is the sort of correlative thinking certain to keep surgery dynamic and of ever-increasing

This thesis was submitted as part of the requirements for the degree, Doctor of Philosophy, May, 1944.

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usefulness to all of mankind. The lower mortality rates (and shortened morbidity) of this era eventuate from many factors, for today's doctor is not only a better operator, but he takes better care of his patients and is, therefore, a better surgeon. At least partial solution of the problems of hydration, electrolyte balance, hemodynamics in shock, intestinal obstruction, and nutrition, among others, are responsible for this improved management of surgical cases.

In all these fields progress has been disproportionately advanced compared with the accomplishments in the dietary care of surgical patients. And, whereas a host of investigators have been concerned with these other complex tasks, a rather small group has dealt with nutritional care. This universal widespread lack of inquisitiveness is unfortunate since more frequently than seems to be appreciated, patients, ill with diseases remediable by surgery, present mild to severe states of starvation or malnutrition. A condition of marginal nutritional imbalance, it appears, may be present in an individual for a prolonged period before the onset of another illness, either of a secondary or unrelated nature. The bodily requirements are thereby augmented above the patient's limited intake, thus making the real need acutely manifest for the first time. There is a broad zone existing between optimal nutrition and classical deficiency states in which abide many borderline cases of unsatisfactory dietary management and/or inadequate food intake. Alertness is necessary, therefore, to detect not only those cases in which the patients are subsisting on manifestly deficient diets but also the instances of occult inanition. During such semi- or starvation states, in both man and animals, survival is at the expense of bodily substance. Man has the capacity to exist in this autocannibalistic predicament for prolonged periods deriving his calorie needs partially or wholly from his own tissues. During this interval, though sustained, he suffers from the compound evils of a diet low in protein content and with the majority of its calories derived from fat. If prolonged, this utilization of a high fat diet, low in calories, simulating as it does so closely experimental conditions in animals, evokes detectable evidence of hepatic dysfunction and hypoproteinemia. Clinical experience has shown that particularly in such cases in man, extensive, prolonged surgical manipulations are poorly tolerated, and occasionally such individuals react unfavorably to relatively minor procedures. They exhibit an instability of blood pressure, disproportionate to any actual hemorrhage during the operation, which responds unsatisfactorily, often, even to transfusions of blood and plasma. During the convalescence the vitality seeps steadily away despite the employment of a variety of therapeutic measures, and, whereas, the pathologist may seem to offer exoneration with the finding of bronchopneumonia or beginning heart failure, in reality the issue was unfavorably settled when the decision was made to operate upon an ill-nourished individual. The fatty liver and hepatic dysfunction developing in such instances and responsible, at least in part, for such tragedies are problems whose significance and remedy are unquestionably of great surgical importance.

Cases 1 and 2 are appended to illustrate just these points and are fairly typical recordings of the tragic sequence of events in patients who have suf-

ferred a large recent weight loss and then had a major operation without adequate provision for nutritional rehabilitation.

CASE 1 (No. 703974).—S. D., aged 47 years, was operated upon elsewhere for an incarcerated ventral hernia which was reduced and repaired; but one month after returning home, a second operation was performed by the local doctor to relieve a recurrent intestinal obstruction. Recovery was slow and incomplete, so that the patient still had signs,

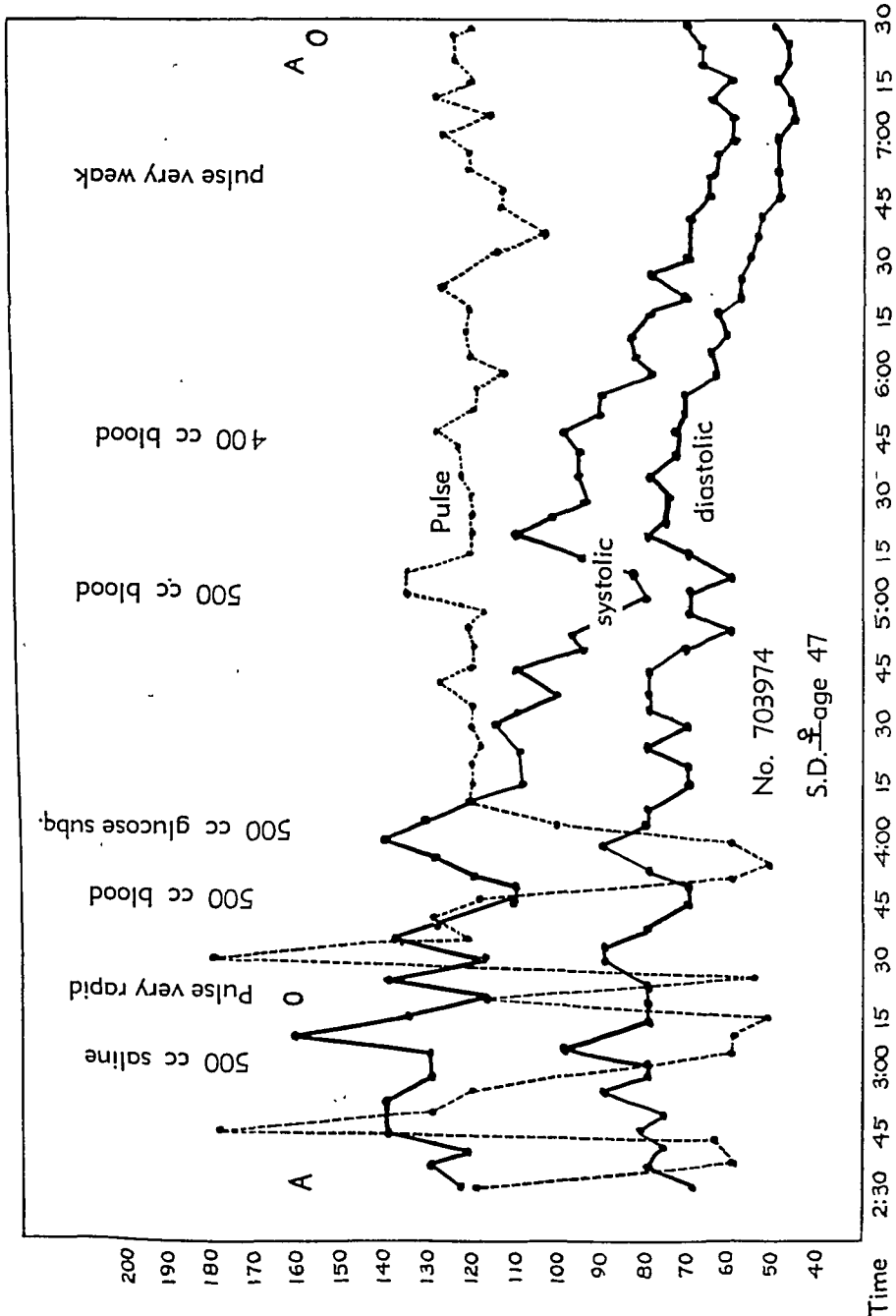


Fig. 1.—Record of blood pressure, pulse, and intravenous fluids during anesthesia (Case 1).

and was suffering from attacks, of intestinal obstruction at the time of her transfer to this hospital. During this interval the patient had lost much weight and had been eating irregularly and in small amounts. Soon after admission, physical symptoms and signs plus x-ray findings of acute small bowel obstruction, of the incomplete and nonstrangulating variety, were present. This condition was treated with intestinal siphonage maintained about two weeks and until shortly before surgery. Whereas electrolyte, fluid, and hemoglobin values were controlled by the appropriate intravenous and subcutaneous therapy, little attention was accorded the protein and caloric requirements. The patient lost an additional 5.4 kilograms after admission and prior to surgery. At the time of operation a partial enterectomy and colectomy were performed to remove the sites of obstruction. During this procedure wide fluctuations in the blood pressure and pulse were noted. The blood pressure was unstable, out of all proportion to the actual blood loss. There was a steady reduction in pulse pressure as can be noted in Fig. 1, despite liberal transfusions with blood and plasma during the operation. In the immediate days postoperative the

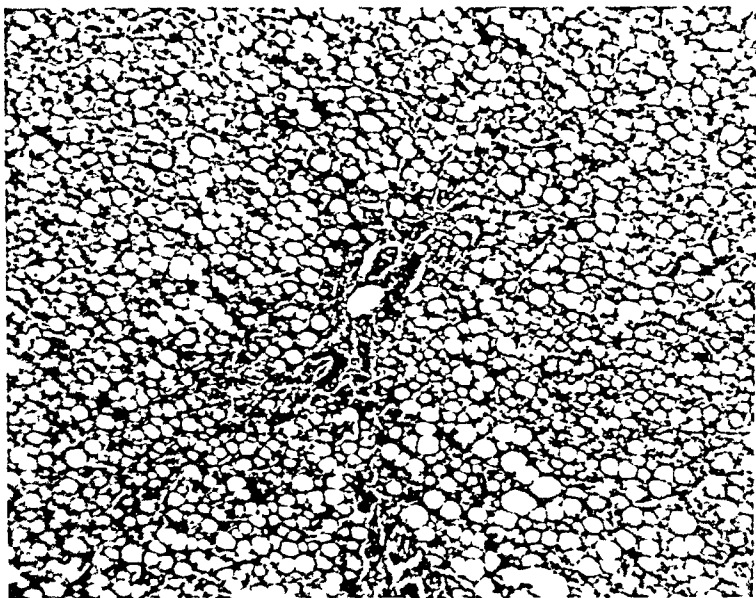


Fig. 2.—Photomicrograph of a section from the liver (Case 1).

pulse rate remained high and the blood pressure exhibited a great lability and a distressing tendency to fall to shock levels. The patient deteriorated steadily and died eleven days later with a temperature of 108° F. The pathologic report was: (1) hepatic insufficiency with marked fatty metamorphosis of the liver (marked degree of this change reproduced in the photomicrograph shown in Fig. 2), (2) jaundice on basis of liver damage, (3) congestive heart failure, (4) pulmonary edema, (5) bilateral hydrothorax and ascites, (6) cloudy swelling of kidneys, and (7) evidence of recent abdominal operation on small and large intestine.

CASE 2 (No. 711332).—E. P., aged 71 years, had, in the five months prior to admission, noticed epigastric distress and fullness, occasional bouts of vomiting, and increasing fatigability, and a fifty-pound weight loss, representing 33 per cent of her total body avoirdupois. The x-ray diagnosis was carcinoma of the stomach. She received plasma, amino acids, and glucose for four days in a quantity sufficient to yield about 1,000 calories and was given also a full liquid diet by mouth. Some of the latter was removed by daily gastric aspiration. A subtotal gastric resection was performed after the four days prep-

aration had restored electrolytes, hydration, and hemoglobin to normal values. During the operation, and persistently afterward, as shown in Fig. 3, the blood pressure displayed a tendency to fall, the pulse was consistently rapid, and the pulse pressure was reduced. These conditions prevailed despite generous repeated transfusions of blood and plasma

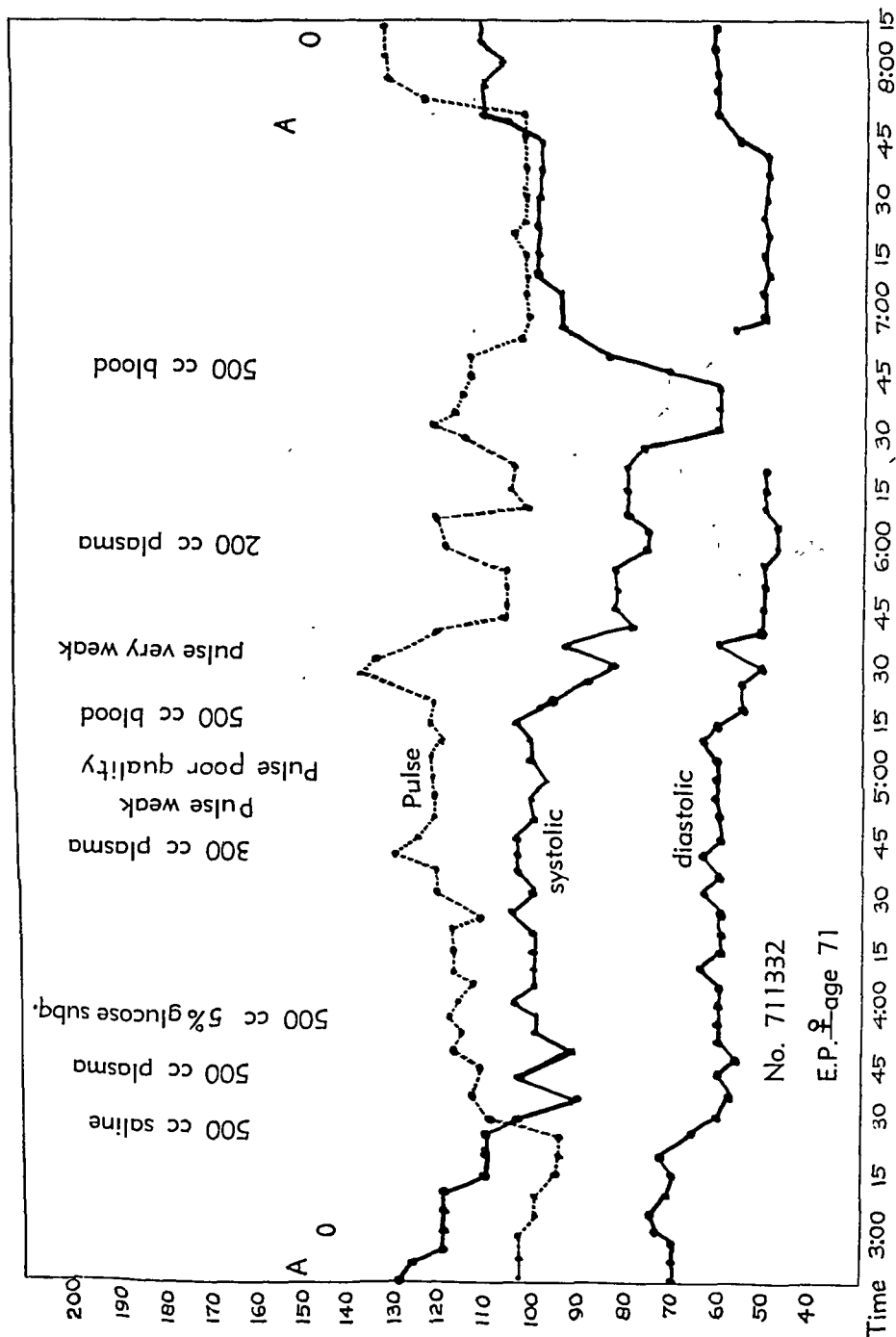


Fig. 3.—Record of blood pressure, pulse, and intravenous fluids during anesthesia (Case 2).

during and after the operation. She died on the third postoperative day. The pathologic report was: (1) moderate amount of vacuolated liver cord cells characteristic of dissolved fat, congestion and atrophy of parenchyma also noted (some of these findings apparent in the photomicrograph, Fig. 4); (2) some congestion and patchy atelectasis of the lungs; (3) evidence of recent abdominal operation with gastric resection.

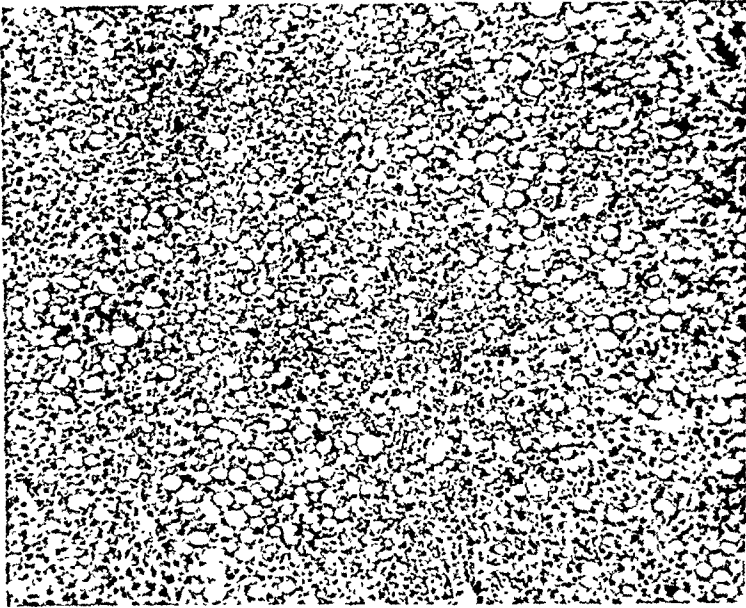


Fig. 4.—Photomicrograph of a section from the liver (Case 2).

Other case histories of this general type could be recorded, and their occurrence within a relatively brief interval served to focus attention upon the inadequacy of the dietary preoperative preparation in such instances. Since the development of a more formal dietary management and with the application of other methods of nutritional preparation outlined in the text of this essay, many patients with weight loss in excess of that reported in cases 1 and 2 have been successfully carried through correspondingly major operations.

#### MORE SPECIFIC STATEMENT OF THE PROBLEM

This study is essentially a clinical investigation. The selected critical control experiments, which can be undertaken by the investigator prosecuting his researches in the laboratory, are not, therefore, available in this study. Proof of the thesis that adequate nutritional preparation of the patient is an item of the greatest consequence must, therefore, rest on the accomplishment of what can be achieved through its employment, especially with reference to an earlier experience when surgeons were content to hydrate their patients adequately, restore electrolyte balance, and adjust the hemoglobin values by transfusions. In a sense, the results have been so gratifying that one may say with a feeling of confidence that, granted adequate nutritional preoperative preparation, in experienced and practiced hands very few patients will

have to be denied operation on the score that they are too poor risks for operation. In other words, the essence of this thesis is that a satisfactory nutritional preparation of the patient will extend the benefits of surgery to a group of patients who in the past frequently have been denied surgery, on the basis that they were too poor risks. Furthermore, extension may be made without pyramiding the risks very much beyond that accepted for the standard-risk patient for a similar procedure. When, during an ever-broadening experience and with an improved orientation in the problem, the benefits of preoperative dietary preparation for the poor-risk patients became so apparent, it seemed reasonable to apply similar methods in a variety of less serious conditions.

In this clinical study, the only criterion for the establishment of a satisfactory objective test of the extent and length of the necessary preoperative nutritional preparation has been the trial and error method. The percentile loss of body weight has served as a satisfactory base line from which to project the length and extent of the preoperative preparation. It is admitted that critical controlled experiments in animals, on this score, would probably be helpful to establish more precisely the length of the necessary period of preoperative preparation. At the same time, however, it must be conceded that results obtained from such a study would necessitate quantitative reconsiderations in the light of species differences and disparities in body size. Fowler and Barer<sup>1</sup> noted that among 105 donors an average interval of 49.6 days was required for the blood hemoglobin value to return to normal after a single donation averaging 550 c.c., and 25 per cent needed nine weeks. Provision for ample iron in the diet shortened this interval somewhat. Studies on dogs bled repeatedly furnish quite different rates.<sup>2</sup> They are capable of regeneration from a severely anemic to a normal status within two weeks after cessation of the hemorrhaging procedure. The hemoglobin rise in these dogs was 5 to 6 Gm. per cent in two weeks, while man needed nearly 50 days to correct a 2 to 3 Gm. per cent deficit.

The interest of the surgeon in the nutritional aspects of patient care relates primarily, therefore, to patients with conditions remediable by surgery who have lost considerable weight, occasioned by the ravages of the disease or who, for one reason or another, present a nutritional deficiency. It is proposed to indicate that it is hazardous to subject patients who have sustained large weight losses to formidable operative procedures after mere restoration of water and electrolyte equilibrium and concurrent adjustment of the hemoglobin to a satisfactory value. It is proposed further to indicate that such patients may be prepared satisfactorily for operation by a feeding of a high protein, high carbohydrate, low fat diet. It is proposed to indicate what the nature of the disability is that constitutes the operative hazard in these patients. Further, the character of satisfactory dietary preparation will be discussed including suggestions for diets which meet adequately the demands of the preoperative nutritional preparation of the patient who has sustained a large loss in body weight. It is proposed to indicate that following satisfac-



tory nutritional preoperative preparation, patients who ordinarily are regarded as poor operative risks may undergo formal operations of magnitude without running risks far out of line with those borne by the standard good-risk patient. In addition to presenting the nutritional problems of the patient who has sustained a large weight loss, it is proposed further to consider the special problems of nutritional preparation of surgical patients with high-grade obstruction at the gastroduodenal opening. The problem of meeting the caloric needs and of preparing nutritionally those patients unable to receive nourishment other than by the parenteral route is to be discussed. The problem presented by bleeding ulcers of stomach and duodenum, with and without obstruction, and in the younger and older age brackets, is to be dealt with in this presentation. Suggestions are to be offered for the nutritional management of patients with disease of the biliary system, especially cases with common duct stone or stricture, or carcinoma of the ampulla or head of the pancreas. The nutritional aspects of a variety of conditions including hyperthyroidism, burns, empyemas, osteomyelitis and other suppurative foci, esophageal lesions (carcinoma or diverticulum), and neoplasms of colon and rectum will be considered. Dietary preparation for surgery in the rarer conditions of gastrojejunoecolic fistula, regional enteritis, and ulcerative colitis will be mentioned.

#### AN EXAMINATION OF CERTAIN ASPECTS OF RELATED LITERATURE

Prior to experiments by Bernard<sup>3</sup> in 1848 indicating that the liver could manufacture sugar when no sugar was present in the diet, it was the prevailing consensus bulwarked by the opinion of the famous contemporary chemist, Jean Baptiste Dumas, that man, unlike plants, had no ability to synthesize bodily fats, proteins, or sugar from those in the diet. Bernard and Barreswil<sup>4</sup> exhibited to the French Academy of Sciences alcohol obtained from sugar, of hepatic origin, by fermentation with yeast. The animal had been fed on meat exclusively and this example refuted, therefore, the hypothesis sponsored by Dumas. In subsequent experiments<sup>5-10</sup> it was shown that an "animal sugar-forming substance" (substance animale glycogène) was present in the liver and was converted to sugar on standing—a material that he later isolated in pure form and which is known today as glycogen. This was found to be identifiable in certain liver cells by virtue of a wine red color-staining reaction with iodine.\* He also noted during experiments involving the livers of animals in various conditions of nutrition and health that this substance was present in lessened amounts in starvation states. Glycogen had been independently isolated one year prior to Bernard's classical experiments by Hensen.<sup>12</sup> Bernard's theory, in the main, is essentially accepted today by modern physiologists, namely, that carbohydrates incoming via portal blood are stored in the liver as glycogen, released to the blood as glucose, and are ultimately metabolized to carbon dioxide and water. During the ensuing two

\*Bock and Hoffman<sup>11</sup> observed that liver glycogen was stainable with Lugol's solution for visualization under the microscope, and is more prominent about central liver cells and scant or absent about the periphery.

decades after the discovery of glycogen by Hensen and Bernard, the subject attracted the attention of many workers, both pathologists and physiologists, and there was general agreement that the state of nutrition was the chief factor determining its presence or absence. In prolonged starvation it would nearly or completely disappear from liver of rabbits, dogs, guinea pigs, hens, and other animals and fowl. Contrarily, an abundance was present when the animal's diet consisted of a plentiful supply of nitrogenous substances and/or carbohydrate. Wolffberg<sup>13</sup> pointed out the significant fact that when the amount of sugar in the diet remains the same, but increased quantities of dried and pulverized flesh (protein) are fed, the glycogen content of the liver is augmented. In addition, Wolffberg,<sup>13</sup> Naunyn,<sup>14</sup> and V. Mering<sup>15</sup> observed an accumulation of glycogen in the liver after an "albuminous" diet, one relatively free from carbohydrate. It was appreciated that the ability of the liver to produce glycogen was dependent on the integrity and the normalcy of the hepatic substance, and that, therefore, a smaller amount would be, and was, present in conditions interfering with the parenchyma, as occurs in fatty livers. This was most marked where the fat content had increased at the expense of the protein component. Saikowsky<sup>16</sup> was unable to find glycogen in livers with fatty degeneration developing after phosphorus or arsenic poisoning. This may have been related in part to the often poor nutrition of such animals. Manassein<sup>17</sup> found the hepatic glycogen content low in febrile states where catabolic processes are accelerated. The anorexia associated with such states customarily leads to a depressed, rather than elevated, caloric intake, so that one could conceive of this representing a form of relative starvation.

Cohnheim<sup>18</sup> noted extensive fatty changes in the chronic wasting diseases as carcinoma, intestinal tuberculosis, and dysenteries. Fatty livers were commented on in noting these changes even in people without fat depots in the panniculus adiposus, mesenteric and omental fat; all depots of fat had disappeared but the fatty liver was still present. He felt these were true "fatty atrophies," that is ". . . the albuminous contents of the affected elements are diminished and partly replaced by fat. . . ." "Fat can and will be produced at the expense of the albumin of the tissue elements—but this represents a proportionate loss of functioning substances." He also commented that this effect can be completely neutralized and effaced with restoration of tissue albumin content, the appropriate remedial measure, but where it is allowed to persist, it is the beginning of the cellular and functional end. Afanassiew<sup>19</sup> presented an excellent experimental study of the problem with many enlightening observations concerning the effects of alterations of the diet on the macro- and microscopic appearance of the liver in dogs. In starvation there was noted a decrease in cell and nuclear size, with the major component of this decrement taking place at the expense of the protein-staining material, and the minor portion accountable by disappearance of some glycogen. Specimens removed after this period of starvation possessed, therefore, an increase in the number of fat droplets within the parenchyma. If a normal animal were fed on sugar or potatoes, preponderantly a carbohydrate diet, the glycogen content

of the liver cells increased but the alteration in cell size was not pronounced. Sustentation with blood fibrin did lead to an actual increase in cell dimensions, but with little attendant glycogen deposition. Alimentation with a diet almost wholly meat produced the largest hepatic cells and they contained the most material taking the stain for proteins. The cellular size alteration with the quality of the food ingested (carbohydrate or protein) was reflected in the liver/body weight ratios. In states of starvation this fell to as low as 1:41, whereas, in animals nurtured on a meat diet it rose to 1:18. The values obtained on the carbohydrate and fibrin diets were intermediate. Atrophy and hypertrophy of hepatic substance in response to dietary influences are apparently here demonstrated for the first time; the significance of this rather neglected phenomenon can hardly be overemphasized.

In the midst of a long and classical paper on glycogen, Pflüger<sup>20</sup> stated that from his observations of the livers of animals maintained upon high protein diets, he was convinced that the liver is an organ for storage of both protein and glycogen. No experiments are cited, and the conclusion appears to arise from personal observations.

Seitz,<sup>21</sup> a student of Pflüger, did perform probably the first crucial experiments to test his theory and showed that in ducks and chickens maintained upon high protein diets there was real enlargement of the liver and increase in its nitrogen content. Tichmeneff<sup>22</sup> completed an even more convincing bit of work in experiments on mice where he found even an increase in protein content of hepatic substance as determined by an increase in the tannic acid precipitable fraction.

Luck<sup>23</sup> stated that each one of the four fractional protein components of liver increased with the alteration from a low protein to high protein diet. This increase was in the order of magnitude of from 50 to 60 per cent. He believed that this was explicable, on the basis of his experiments, as both a hypertrophy and a hyperplasia with an actual increase in protein content per unit weight of tissue. All the liver proteins appeared to participate freely in the storage function.

As suggested previously, hepatotoxins other than starvation are capable of effecting gross histologic and functional changes in this organ. The agent most extensively studied by investigators has been chloroform. This has probably been related to the gratifying reproducibility of the experimental conditions and results, the correlation between duration of anesthesia (or more quantitatively expressed as the amount of the drug ingested) and the pathologic findings under controlled conditions, and finally to the experimentally induced situations which mirror so closely the disastrous clinical counterpart met with occasionally in patients anesthetized with chloroform. Casper in 1850, soon after introduction of the drug as a general anesthetic, associated the possibility of death some time after its use, with a delayed action of chloroform. Nothnagel in 1866 related evidence to show that chloroform might produce fatty changes in the liver. Case reports then appeared in the literature

suggesting that this drug was responsible for death as a delayed manifestation of its toxicity, in distinction to its recognized capacity for producing cardiac arrest during the period of any administration. Rosenbaum,<sup>24</sup> while investigating a number of agents injurious to the liver, found a depletion of hepatic glycogen after chloroform anesthesia. Rosenfeld<sup>25-28</sup> demonstrated that animals fed on carbohydrate were, in the main, less susceptible to all those drugs producing fat accumulations in the liver. It was his contention that after such a poisoning (chloroform) the capacity of the liver for either protein or fat metabolism was more seriously impaired than for carbohydrates. The injured liver cells he felt could utilize carbohydrate, but with this constituent exhausted, the cells starved and exhibited obvious damage. The body in its futile attempt to use fat ultimately led to the local deposition, encountered under such circumstances, in the liver. Finally, he thought that the detoxifying capacity (entgiftenden fähigkeit) of the liver was positively correlated with its glycogen content. Beddard<sup>29</sup> grasped the significance of this biologic information and translated the suggestions into clinical therapy. At that time anesthetization with chloroform was in common use among English surgeons. He counseled before surgery, and especially where there was the possibility of hepatic glycogen depletion, as in the case of "rickety or ill-nourished children," that the diet include excess amounts of carbohydrates. It is difficult to understand how such an intelligent analysis of the similarity between animal experimentation and observations in man could have been so generally ignored by the healing profession. Wells<sup>30</sup> studied in detail the clinical findings, gross and microscopic anatomic changes, and chemical alterations in a fatal case of delayed chloroform poisoning. Among other considerations he emphasized the presence of an increased percentage of fat in the liver. It was his suggestion that as in the Meyer-Overton theory of anesthesia, the lipids of the liver take up the chloroform, which acting as a cell toxin interferes with normal functions. The amount of chloroform withdrawn from the blood, he hypothesized, would be proportional to the hepatic fat content, and therefore when increased amounts of fat were present the greater would be the cellular intoxication. Opie and Alford<sup>31-33</sup> resumed the attack on the problem from the nutritional sector. Employing white rats, poisoned with accurately measured amounts of chloroform, they studied the effects of qualitative alterations in the diet upon the mortality rate and found those animals fed a high carbohydrate mixture acquired a significant degree of protection. A meat diet was less effectual and where the diet was largely fat, all animals died under the conditions of the experiment. Any diet including fat in the caloric content immediately raised the mortality rate for that group. Whipple and Speed<sup>34</sup> found while studying the effect on liver function of therapeutic doses of a group of anesthetics and narcotics that all were capable of producing demonstrable evidence of impaired liver function as measured by a dye-clearance technique. Chloroform was noted to produce the most severely depressed function in the group where ether, alcohol, paraldehyde, chloral, and urethane were also studied. In an earlier investigation, Whipple<sup>35</sup> had been able to produce regularly, with chloroform anesthesia, a

necrosis of the central portion of each hepatic lobule in dogs, roughly proportional to quantity of the drug administered, as had other workers, but was surprised to note the frequent absence of such phenomena in the fetuses of pregnant dogs exposed to chloroform. This protection seemed to last about three weeks, and ably protected animals exposed to chloroform anesthesia at any time during this interval. A hyperglycemia with both ether and chloroform anesthesia was recorded, and this was associated with a reduction in hepatic glycogen. Graham<sup>36, 37</sup> sought the cause of this increased safety to chloroform anesthesia during the neonatal period and related it to the abnormally high glycogen content of the puppy liver compared to standard values for adult dogs, a value which spontaneously falls to a normal one in about three weeks after birth. He secured evidence favoring this concept, by producing a postchloroform hepatic necrosis resembling that of adult dogs among puppies who had had their glycogen stores depleted by starvation or phlorization. Under these circumstances the increased resistance to the drug was no longer present. Four papers by Davis and Whipple, and Davis, Hall, and Whipple<sup>38-41</sup> shifted the emphasis from the beneficial effects ascribed to an increased carbohydrate intake and an augmented hepatic glycogen content to the role of protein in protecting the liver exposed to chloroform. This originality of approach to the problem of hepatic damage, including methods, idea, and food substances tested is clearly set forth in these papers by the Whipple group—papers that merit the distinction and respect due all classics, but much credit is similarly due Ravdin and his associates for initiating the clinical application of this fundamental knowledge. The experiments performed were numerous, the results and conclusions often unequivocal and self-interpreting. Only a few of the observations that seem most pertinent are to be cited:

1. Starvation materially increased the susceptibility of animals to chloroform. "A maximal injury is to be expected."

2. Sugar or richly carbohydrate diets, skimmed milk alone, commercial casein alone, or in combinations with a cracker meal, fed but a few preanesthetic days to the animals furnished maximal protection to the liver. An acid digest of casein administered a few minutes prior to the exposure to chloroform vapors appeared to offer some protection. Proteins from gelatin, heart, and skeletal muscle had only slight protective action.

3. They clearly stated, "The hypothesis that glycogen protects the liver cell against the injury of chloroform will not explain all the observed facts," and concluded that other factors must play a role.

4. The benefits from carbohydrate in the diet during the repair of hepatic injury due to chloroform accrue from the protein-sparing action of the carbohydrate, by virtue of "conservation of protein split products."

5. A diet of bread and skimmed milk evoked the optimum repair after a standard amount of chloroform injury. Other diets of cooked muscle or organs were less efficacious. Diets of fat, offered no assistance (more than was present during starvation) to liver regeneration.

Interesting speculations are initiated by a rather detailed perusal of the appended protocols and discussions. There was a tendency to flabby clot formation and even prolonged bleeding from biopsy sites. Doyon<sup>42, 144</sup> had noted earlier a similar phenomenon after chloroform anesthesia. Whipple and Hurwitz<sup>43</sup> demonstrated that there was an impairment or cessation of fibrinogen formation by the liver after injury with chloroform. Brinkhous and Warner<sup>44</sup> were to complete the explanation thirty years later in terms of hypoprothrombinemia ensuing after chloroform anesthesia, a hypoprothrombinemia which fails to respond to vitamin K until the hepatic parenchyma has recovered. In addition, it was noted by Davis and Whipple that after celiotomy for liver biopsy there was often an impaired wound healing associated with the experiments employing limited diets. This occurrence probably was related both to deficient plasma proteins and to inadequate vitamin C intakes. A more complete handling of this aspect of the nutritional problem will be considered later. If the calories and composition of the diets of Davis and Whipple had been calculated, then been made both ample and isocaloric, it would have quieted the valid objections certain to arise, for a part of the hepatic necrosis after chloroform anesthesia appeared in animals on diets obviously inadequate calorically, and which hence might be expected to suffer in this situation by virtue of the inadequate nutrition, a factor known to influence most unfavorably the hepatic tolerance for this drug.

Glycogen and protein appear, therefore, to potentiate natural hepatic resistance. The mechanisms responsible for this could be several:

1. Both substances are lipotropic, with glycogen less effective, and merely displacing fat already deposited. Protein actively removes fat from the liver parenchyma.<sup>45-50</sup>

2. Each might restore materials vital for cellular metabolism, as for example in the specific sense of a detoxifying substance or as an as yet unrecognized non-specific material.<sup>51</sup> Xanthine, or its sodium salt, was found to influence favorably the prevention of acute or chronic hepatic changes after exposure to the toxin carbon tetrachloride. Ravdin, Vars, and Goldschmidt<sup>52</sup> employed sodium xanthine and obtained some protection for the liver after chloroform anesthesia. They felt it was related to the local tissue reaction induced by this substance. Hepatic glycogen has been suggested as the source of the detoxifying compound glucuronic acid.<sup>53-55</sup> Miller, Ross, and Whipple<sup>56, 56a</sup> described a distinctly enhanced protective action with methionine and cystine in dogs made hypoproteinemic, fed these amino acids, and then exposed to chloroform. It was their impression that this was a specific action related to the SH group, sulfhydryl radical, present in, and essential for, certain hepatic detoxification processes which tend to spare other enzymes, normally present, associated with oxidation-reduction systems in the liver cells, as glutathione for example. Chloroform may be inactivated by these systems which during the process exhaust the quantity of interacting compounds, particularly if partial depletion has obtained previously because of a deficiency state. This permits competition between chloroform and normal respiratory mechanisms thereby interfering with the oxy-

generation necessary to prevent hepatic necrosis and autolysis, or at least permitting a functional depression with the accumulation of bodily substances customarily eliminated and detoxified by the liver. Contrarily, an excess of the sulfydryl groups, indispensable for the synthesis of the detoxifying product, can be brought about with the addition of methionine or cystine to the diet, or more deviously, by feeding casein which contains these amino acids. With such a theoretical excess present the chloroform hazard actually, in experiments designed to test this concept, appeared nearly nullified. Beattie and Marshall and associates<sup>220-222</sup> have sought to evaluate clinically methionine as a therapeutic aid in patients with liver damage from infective hepatitis and one instance of carbon tetrachloride poisoning. The material was supplied to their patient orally and intravenously. Even admitting the limitations imposed by the meager quantity of data available, since the results achieved were so favorable in the patients appropriately selected for such therapy, the perhaps premature surmise is hazarded that in the near future this amino acid is destined to assume a truly vital role in the restoration of function to livers damaged, through fatty metamorphosis or other hepatotoxins, but not destroyed as in advanced cirrhosis and severe acute atrophy.

3. Glycogen by conversion to glucose could exert its well-known protein "sparing" action either at the source<sup>32, 40, 57</sup> and thus reduce the amount of protein autolyzed or in a more peripheral fashion and "spare" the conversion of amino acids to energy units, permitting a more liberal utilization in the normal anabolism. More words than wisdom have been written in frequent and occasionally bitter polemics which have attempted to resolve, either on paper or in the laboratory, these issues cited, into primary effects and contributing action.

Moise and Smith<sup>58, 59</sup> found protein more effective than carbohydrate as a substance for inducing hepatic protection after exposure to chloroform. Goldschmidt, Vars, and Ravdin<sup>60</sup> then explored this possibility, namely, that the protein component of the diet is of more fundamental importance than the carbohydrate fraction in the development of hepatic protection against chloroform anesthesia. They studied the effects of this drug on white rats, "because of the ease of attainment of adequate maintenance and growth on diets predominating in one or another of the foodstuffs," and then fed several variations of these diets to the animals, including those with very high carbohydrate, mixed carbohydrate, protein and fat content, high protein low fat or high fat, and high fat without protein. After a prolonged subsistence on the selected regimen the animals were exposed to chloroform vapors in a standard fashion and then sacrificed at the end of twenty-four hours. The livers were studied chemically for glycogen and fat, and microscopically for both these as well as the cytologic reactions of degeneration and necrosis. The authors wisely refrain from sweeping generalizations about these experiments but do propose the following interpretations of the supplied data:

1. Within a constant range of hepatic lipid content, in animals on similar protein intakes, a high hepatic glycogen content per se fails to provide protection.

2. Under their experimental conditions, a direct linear relationship exists between hepatic lipid content and the incidence and severity of the damage to the liver following chloroform anesthesia.

3. This effect is independent of the glycogen content but can be attenuated by a previous feeding of a high protein diet, and obtains in instances of high hepatic lipid content. Conversely, starvation aggravates the damage normally accomplished by a chloroform anesthesia, an effect additionally potentiated by a high lipid content in the liver of the starved animal. Casein, as in the experiments of Davis, Hall, and Whipple,<sup>41</sup> was the protein selected to fortify these diets. Messinger and Hawkins<sup>61</sup> confirmed the work of Schiffrin,<sup>62</sup> who noted a minimizing of the arsphenamine injury to the liver in animals fed a protein as compared to a fat diet. Histologically, regeneration was more rapid and complete with the former. In addition, dogs on the high fat diet exhibiting manifest liver injury (elevated icterus index) and a reluctance to eat promptly displayed an improvement and regression of the hepatic dysfunction when changed to a high protein or carbohydrate diet. Miller and Whipple<sup>63</sup> studied the effect of chloroform on animals made hypoproteinemic by plasmapheresis or diet and came to the conclusion that the severity of the injury to the liver in these dogs after such anesthesia paralleled the depletion of liver and body protein. Quite minimal insults from light chloroform anesthetization for short periods of time (fifteen to twenty minutes) were fatal to the majority of such canines, while control animals tolerated ninety minutes of such exposure with but little liver injury. This enhanced susceptibility in the depleted dogs could be corrected, it appeared, at least in part, and at times completely, by a single large feeding of protein (meat) thirty-six hours prior to the anesthesia. Dogs depleted of proteins by plasmapheresis uniformly gained some protection against liver damage when nourished with a richly protein diet. They could not tolerate the same amount of chloroform as normals but convalesced significantly superior to those depleted animals not so selectively alimented.

There may be no satisfactory single explanation available, on the basis of our admittedly limited present knowledge, and assuredly it is difficult to arrive at the common denominator for the effects produced by chloroform anesthesia in a liver with a high lipid concentration—actions which are potentiated by starvation or hypoproteinemia, and inhibited either by a high hepatic protein content or feeding before the exposure of a full protein dietary supplement. However, at the risk of indulging in oversimplification, the impression exists that this phenomenon so intimately related to cellular metabolism may be but a manifestation of anoxia. In partial support of this thesis is the recognition and general acceptance that chloroform interferes with oxidation—reduction potentials (*vide supra*). Additionally, Goldschmidt, Ravdin, and Lucke<sup>64</sup> found that vaporizing chloroform with oxygen rather than air decreased the damage produced by this drug on the liver, and that this deleterious action could be inhibited (by breathing high concentrations of oxygen) even where livers had a high lipid content. Schneedorf and Orr<sup>65</sup> found a depression of the liver function, bile formation, with anoxia and a prompt



return at an increased rate after the administration of 100 per cent oxygen. It might be predicted that since most of the blood coming to the liver has passed through a set of capillaries and is already venous, that as it traverses the second set, the oxygenation, being additionally reduced, is at a critical level and only a meager oxygen reserve remains available. Warren and Brannon<sup>66</sup> obtained blood directly from the hepatic veins in man and after measuring the oxygen content found it was lower there than in samples obtained from the auricle. In addition, the situation is made even more critical, and the tolerances further reduced, because in this tissue with an, at best, low tension of the oxygen essential for anabolism, there exists according to Bradley<sup>67</sup> the highest rate of intracellular proteolysis (catabolism). This contention is clearly substantiated by the experiments of Addis, Poo, and Lew,<sup>68</sup> who noted that of all the body proteins, liver had the largest percentage loss during a brief fast. Here, with protein absent from the daily intake, the counterbalancing of autolysis by synthesis is at a serious disadvantage.

This summary of a proposed theory relating ultimately the ill effects of chloroform to local anoxic states is, therefore, offered.

1. Fat contributes to the anoxia by two mechanisms:

- (a) It attracts and holds an abnormal amount of chloroform compared to the other tissues with lower fat solubility coefficients, and hence a greater quantity of this drug is available to depress the respiratory enzyme system, more completely, and for a longer interval of time.
- (b) It acts as a diluent of other constituents and thereby increases the diffusion distances for entering oxygen and outgoing, frequently toxic, products of metabolism.

2. Glycogen favors adequate oxygenation through its mildly lipotropic action and by increasing with its protein-sparing power the quantity of protein available for cellular metabolism.

3. Protein prevents anoxia because of its strongly lipotropic capacity and because the natural respiration of a normal cell depends primarily upon an adequate available complement of protein.

The conclusion is also reached that these apparently pathologic states are likewise reversible, under appropriate conditions, and are interpretable, therefore, as exaggerated expressions of a labile and dynamic equilibrium. The effects of high or low fat, carbohydrate, or protein diets find representation in functional and, frequently, microscopically visible states, often reversible, and whereas the intake of a high protein-carbohydrate diet has the capacity to shift this reaction in the direction of intracellular synthesis and a normally functioning, nonpathologically involved mechanism, unfortunately quite the opposite obtains when the liver is injured by semi- or starvation states and other more powerful chemical hepatotoxins.

#### LITERATURE CORRELATING NUTRITIONAL CARE WITH CLINICAL MATERIAL

An appreciation of the importance of nutrition in clinical cases which resemble the experimental conditions just described has not been totally lack-

ing but does seem, compared to the possible significance, to have been disproportionately meager. Often the emphasis has been preponderantly on the dysfunction from an hepatitis associated with biliary tract disease.<sup>69-76</sup> Graham<sup>69</sup> re-emphasized under such circumstances the significance of faulty dye clearance by the liver, at the time of cholecystography. When seriously impaired function was demonstrated, in this fashion, the patient was prepared for several days with additional amounts of glucose intravenously. With such therapy he was able to curtail the mortality of cholecystectomies at his clinic by 90 per cent.

It does not seem pertinent to discuss at length the several papers which tend to obfuscate issues at best already somewhat less than clear. For instance, Soskin and Hyman<sup>77</sup> in an article abstracting a number of papers by Soskin on this problem, without an inferred or direct reference to the total caloric intake, stated that intravenously administered glucose is superior to oral carbohydrate, "to protect a damaged liver by means of deposition of glycogen therein." Sears and Banks<sup>78</sup> expressed a similar conviction in the matter of intravenous versus oral feeding of sugar, and both groups are categorically certain of the prime, almost exclusive, importance of carbohydrate. . . . "Acute and chronic destructive and degenerative processes of the hepatic parenchyma are best treated with large amounts of carbohydrate," to quote the former group, and "cellular repair of the liver is best facilitated by a carbohydrate diet," affirmed Sears and Banks. These two statements ignore the most basic fundamentals of tissue healing, and the local necessity for protein, for under such circumstances as those outlined, the sole source of nitrogenous material for regeneration would be from endogenous metabolism. This admittedly contributes a component to the anabolism, as indicated by Davis, Hall and Whipple,<sup>41</sup> but the addition of protein to the dietary intake ordinarily supplies the preponderant fraction of the quantity required. Also, the unqualified statements of these groups relative to the superiority of intravenously injected glucose over that provided through the oral route overlook the stringent caloric limitations imposed when venoclysis is the sole avenue for nutrients to enter. It is barely possible to provide the minimum caloric needs for basal conditions in adults by this method, and to conceive of effecting any appreciable storage is not heeding reality. Until the work of Goldschmidt, Vars, and Ravdin,<sup>80</sup> this general plan represented approximately the maximum nutritional preparation of surgical patients with biliary tract disease. In 1939 this group called attention to the necessity of providing extra protein in a diet to be fed preoperatively. The diet recommended contained 74 per cent carbohydrate, 20 per cent protein, and 6 per cent fat in sufficient quantity to yield 3,000 calories daily in three meals and three interval feedings. The high carbohydrate content was found to be well tolerated by patients. The protein in large measure consisted of casein in the form of cottage cheese, skimmed milk, and Casec.\* Biopsy specimens, obtained from patients given this diet five or more days preoperatively, contained uniformly less hepatic fat than material

\*A proprietary preparation of Mead Johnson and Company, Evansville, Ind.

from a comparable group of patients not given this diet. An inverse relationship between glycogen content and liver fat was not encountered, that is, several instances of a heavy degree of fatty infiltration were associated with the highest hepatic glycogen concentrations.

Many investigators and clinicians interested in the problems of hyperthyroidism have related the thyroid storms and deaths postoperatively to hepatic damage or correlated hyperthyroidism with hepatic failure.<sup>79-88</sup> Shaffer<sup>89</sup> in the autopsying of patients with hyperthyroidism found convincing evidence of histologic changes, especially loss of liver substances and fatty infiltration. The hippuric acid liver function test has been employed in the detection of hepatic dysfunction developing in this condition.<sup>80, 88</sup> Preoperative clinical improvement in the patients was paralleled by a return of the conjugation values toward normalcy and postoperatively pathologic levels were common. It has been appreciated for many years that the administration of thyroid hormone to animals resulted in a low level of hepatic glycogen,<sup>90</sup> that an elevation of the level was difficult to obtain,<sup>91</sup> and that such animals had an increased susceptibility to hepatotoxins.<sup>92</sup> The customary method of feeding hyperthyroid patients was presumably influenced unfortunately by this, therefore preparation emphasized only carbohydrates in the preoperative nutrition. Attention might profitably have been focused also on the tremendous protein needs developing under such circumstances.

Coleman,<sup>94</sup> and Boyce and McFetridge<sup>95</sup> at about the same time found that patients with apparently normal hepatic function sustained a drop in function, occasionally to a marked degree, regardless of the variety of anesthesia, after the relatively simple operations like elective hernioplasties or appendectomies. In some instances wherein hepatic damage was noted preoperatively, a dangerous impairment of liver function was exhibited after anesthesia and surgery. Ravdin<sup>96</sup> stated, "When the concentration of liver fat increases about the normal, and the reserve stores of protein are seriously reduced, liver necrosis is apt to occur when the patient is subjected to a variety of anesthetic agents, regardless of the hepatic glycogen level." Abels, Rekers, Binkley, Pack, and Rhoads<sup>97</sup> studied fifty proved cases of carcinoma in the gastrointestinal tract. Each patient was examined for evidence of hepatic dysfunction by means of eight tests. Ninety-eight per cent displayed an abnormality in two or more tests, 86 per cent had three or more tests in the pathologic range. Among twenty-five normal adults investigated by the same tests for hepatic function, two individuals had a maximum of two tests recording abnormal values. The tests employed were determinations of the plasma prothrombin, serum bilirubin, serum proteins (total and fractionation into albumin and globulin), plasma vitamin A level, urinary excretion of glucuronates, mean corpuscular volume of erythrocytes, urinary and fecal excretion of urobilinogen, serum cholesterol, and cholesterol esters. The advantage of selecting multiple tests is apparent. Any one alone provides but a crude index of the functional state of the liver, whereas, with a number of tests one can secure information on the numerous independent physiologic functions of this organ, and thus values can be secured which more closely approximate the actual hepatic capacity.

This demonstration of a depression of two or more indices of hepatic function, in so large a percentage of the total number of patients with gastrointestinal disease, seems particularly significant. Frequently it is precisely this individual, with such a case history, laboratory findings, and diagnosis of a gastrointestinal cancer, who requires a very major type of surgery. The failure to recognize, treat, and correct such hepatic derangements is certain to pyramid the risks of anesthesia and of the operative manipulations, to hamper wound healing, and thus ultimately to increase the mortality rate of this group.

#### DISCUSSION OF MECHANISMS OF HYPOPROTEINEMIA

Hepatic dysfunction and the fatty liver developing in surgical patients are problems unquestionably of great prognostic significance; their remedy is of paramount therapeutic consequence. At times, the many perplexities connected with an analysis of the mechanisms producing hypoproteinemia appear to be closely woven into these same considerations; in other instances hypoproteinemia develops from diverse causes. On all occasions it arouses an equivalent interest and is as important to the whole dietary problem as hepatic dysfunction and the fatty liver. The following is proposed to furnish some orientation into the mechanisms concerned with the development of hypoproteinemia:

*Increased Rate of Catabolism.*—Hypoproteinemia may result from an increased rate of catabolism, that is, the combustion of body protein takes place more rapidly than normal and, unless compensated by augmented intake, at the expense of protein stores. The increased excretion of urinary nitrogen, noted during febrile states, is the best example. Here the wasting process is rapid and promptly leads to a negative nitrogen balance, unless treated. It is rather unorthodox to consider hyperthyroidism in a discussion on hypoproteinemia, yet here too the protein needs are sharply increased. More fortunately than in the hyperthermias, where anorexia is the rule and secondarily reduces the protein intake, here the appetite is customarily enhanced and some compensation of intake, therefore, takes place. The adjustment is frequently inadequate, however, because the tempo of metabolism under the driving influence of thyroxin is so rapid that destruction of the individual's own tissues takes place. The percentage of total body weight lost recently is of the gravest significance in the preoperative evaluation. Therefore, the diet of the thyrotoxic patient should provide increased amounts of all basic elements with the emphasis on the protein and carbohydrate components. The metabolic problem in hyperthyroidism is complicated further by the depression of hepatic function and an increased sensitivity to hepatotoxins (*vide supra*). This is, therefore, another reason to include in the diet ample supplies of proteins with a high biologic value that body repair and regeneration be effected with the greatest expediency.

*Increased Rate of Loss.*—Hypoproteinemia may result from an augmented rate of protein loss. For example, early from a burned area copious quantities of protein are lost in the fluid weeping from the myriads of injury capillary walls no longer impervious to protein seepage. Large amounts also are

sequestered into the tissues locally, yet probably most of these eventually accumulate back in the circulating blood via the lymphatics. Temporarily, however, their absence does contribute to the acute hypoproteinemia of burns. Later, in the history of a burn, protein is lost both by the exudation of plasma from extensive, granulating unepithelialized burned areas and through the richly protein cellular discharge of leucocytic elements from this site. And the stores are depleted still more by the increased requirements relative to healing and repairing the cutaneous defects produced by the burn.\* Other frequent surgical problems with abnormal protein loss are: following hemorrhage, during peritonitis, in small bowel intestinal obstruction (particularly the strangulating varieties), and in chronic ulcerative lesions of the large and small bowel. Less obvious examples are found in the protein character of exudates from abscesses and empyemas. The purulent discharge from a spacious suppurative pleuritic cavity may amount to several hundred cubic centimeters daily of fluid with a protein concentration of 8.1 to 21 Gm. per cent and may contain 4.6 to 11.5 Gm. per cent of albumin.<sup>95, 99</sup> Thus, much protein is commandeered from the circulating stores and depots, which a febrile and anorexic patient can ill afford, either in terms of his reduced dietary intake or by virtue of the depressed hepatic function associated with such infectious states. The loss may be largely renal, as in nephritis, nephrosis, or amyloid disease. A single large or multiple smaller decubitus ulcers are capable of easily producing a serious unfavorable nitrogen imbalance. The tremendous amount lost by repeated paracentesis for ascites simulates closely the experimental plasmapheresis technique. Quite as easily it is capable of inducing severe hypoproteinemic states. In constrictive pericarditis with ascites treated by repeated aspirations the hypoproteinemia has been wrongly stated to be of hepatic origin. The protein content of such fluid is customarily small (1 to 2 per cent) but because of the several liters removed at each sitting, the total protein loss is large, especially since it is predominantly albumin. Therefore, actually, the liver may be producing the colloid protein at better than a normal pace.

*Decreased Protein Intake.*—Hypoproteinemia may result from a nutritional deficiency. That is, it may develop through poor selection, unavailability (war edema), a frank reluctance or disinclination to partake of food, or some defect in absorption as characterizes conditions like sprue, pellagra and occasionally pernicious anemia, the nonspecific diarrheas of infancy or bacterial ones of adulthood, and gastrocolic and high intestinal fistulas.

*Reduced Capacity of Fabrication.*—Hypoproteinemia may result from a reduced capacity or actual failure of protein fabrication by the liver. Acute, subacute atrophy, biliary (Hanot's), and portal (Laennec's) cirrhosis are the outstanding examples of this mechanism. Actually, the protein synthesis is probably depressed to varying degrees by all agents inducing a hepatitis, that is, sulfonamides, arsenicals, anesthetics, shock, bacteremia, viremia, septicemia.

It is admitted that this outline which has been proposed for the several fashions by which hypoproteinemia may develop possesses inadequacies. For

\*An additional expression of the thermal injury could be an actual hampering of conversion, by the body, of amino acids to fabricated proteins, as proposed in the post-traumatic theory of abnormal nitrogen loss.

instance, the reader may well recollect mechanisms producing hypoproteinemia which have not been included. Also, at times, certain conditions may seem to have been arbitrarily placed under one heading rather than another. In addition, and this is to be emphasized, one or more causes for depletion may co-exist and simultaneously effect unfavorably the plasma proteins. That is, low values ascribable to an inadequate caloric intake will be secondarily reduced through the agency of ulceration, hemorrhage, and sepsis, and tertiarily depressed by a concomitant reduction of hepatic function. Even with these imperfections inherent in this outline, it is felt that by so cataloguing the broad range of events contributing to the development of hypoproteinemia, its genesis will attain a clearer appreciation.

#### DISCUSSION OF THE EFFECTS OF HYPOPROTEINEMIA

Many ills and complications of postoperative convalescence are said to stem from hypoproteinemic states. The following are the more clearly chargeable to such a reduction in plasma protein. There may be impaired wound healing or even disruption. Delayed intestinal motility, even intestinal obstruction, and anastomotic stomal difficulties have been noted. Edema formation can supervene, and related to this are quite likely some of the postoperative bronchopneumonias. A decreased resistance to infections with a reduction in antibody formation has been described. Probably also a decreased tolerance to shock-producing circumstances exists. Certain chronic anemias appear related to an inadequate protein intake. Other miscellaneous conditions have been ascribed to this condition. Clark, after studying the effects of diets on wound healing, inferred from feeding a high protein diet to dogs that this abolished the quiescent or lag phase in their wound healing. Harvey and Howes rather felt that the inception of the healing process did not occur any sooner on a high protein diet, containing 80 per cent casein by weight, but believed the velocity of fibroblastic growth was more rapid and that maximum healing was reached sooner under these conditions. The work of Clark,<sup>100</sup> and of Harvey and Howes,<sup>101</sup> is, therefore, a somewhat practical application of the fundamental researches of Osborne and Mendel<sup>102</sup> and of Rose.<sup>103, 104</sup> These workers clearly indicated the utter essentiality of certain amino acids for normal growth processes. Arey,<sup>105</sup> reviewing the problem of wound healing, concluded that many of the most important factors associated with repair were more or less directly related to or dependent upon a diet high in protein. Thompson, Ravdin, Rhoads, and Frank<sup>106, 107</sup> confirmed the finding of earlier workers of delayed fibroblastic proliferation in hypoproteinemic dogs, but were able to prevent this reparative delay by elevating the colloid osmotic pressure, after the incision was made, employing lyophilized plasma. Clinically there is recorded an increased incidence of wound disruptions in hypoproteinemic individuals. Rhoads, Fliegelman, and Panzer<sup>108</sup> related the mechanism of delayed wound healing in hypoproteinemic animals directly to the reduced colloid osmotic pressure. This, they believed, was the most satisfactory explanation for normal fibroplasia in dogs, made hypoproteinemic (by plasmapheresis or other methods), in whom the total colloid osmotic pressure was raised to

approximately normal values by the intravenous injection of the metabolically inert material, acacia. Sokolov<sup>109</sup> and, somewhat later, Lanman and Ingalls<sup>110</sup> indicated the importance of adequate amounts of vitamin C for normal wound healing. They felt this consideration was an important biologic factor in normal regeneration. Taffel and Harvey<sup>111</sup> confirmed these findings. Hartzell, Winfield, and Irvin<sup>112</sup> were inclined to credit hypoproteinemia with at least as an important a role in the reunion of operative sites. While appreciating the value of vitamin C in repair, they pointed out in their cases that in each instance of disruption, hypoproteinemia was associated. A rather interesting possible causal relationship between vitamin C deficiency and protein genesis was hinted at in two papers by Levine, Marples, and Gordon.<sup>113, 114</sup> An inability to metabolize the amino acids tyrosine and phenylalanine, which developed spontaneously in an infant, was corrected, they noted, by the use of ascorbic acid. In summary, it seems reasonable to opine that with either a plasma protein lack or ascorbic acid deficiency, wound healing is retarded; with both reduced, the felony is compounded.

Jones and Eaton<sup>115</sup> were among the first to relate malfunctioning gastroenterostomy stomas to postoperative nutritional edema. They appreciated that the latter was related to the malnutrition, starvation, hemorrhage, and purulent discharges which were not uncommonly the lot of surgical patients. Unfortunately, the incomplete, and hence with respect to tissue repair well-nigh valueless, protein, gelatin, was selected for fortifying the proposed corrective diets. Meecray, Barden, and Ravdin<sup>116</sup> noted a profoundly delayed emptying time occurring in intact stomachs or the residual pouch after resection. They suggested this was caused by hypoproteinemia. It was felt that the "vicious circle" effect (Barden Ravdin, and Frazier<sup>117</sup>) after gastroenterostomy could be relieved in certain instances by transfusions. Davis and Getzoff<sup>118</sup> found instances, simulating adynamic ileus they believed to be caused by hypoproteinemia, which were corrected by transfusions.

Starling<sup>119</sup> was the first to hypothesize a fluid circuit between the blood stream and the extravascular spaces in which the distribution of liquid was regulated largely by a finely adjusted balance between hydrostatic pressures and the colloid osmotic forces. The range of normal values of the plasma proteins producing this force, according to Furey,<sup>120</sup> is:

	AVERAGE	RANGE
Total proteins	7.36	6.2 to 8.1
Albumin	4.92	4.1 to 5.8
Globulin	2.40	1.7 to 3.5

Per gram, the albumin fraction contributes 5.5 mm. of mercury and the globulin fraction 1.4 mm. of mercury osmotic pressure, under normal states of hydration.<sup>121, 122</sup> However, when the plasma proteins are reduced in concentration, as in hypoproteinemia, each gram has less osmotic force, and as might be anticipated when there is increased protein concentration, as in dehydration, each gram exerts more force than it does at normal concentrations.<sup>123-125</sup> A total osmotic force of circa 17 mm.<sup>126</sup> of mercury is necessary to prevent

edema formation with normal hydration. Bruckman and Peters<sup>127</sup> noted edema when albumin concentration fell below 3 Gm. per cent, with adequate hydration. Moore and Van Slyke<sup>128</sup> stated the critical concentration of total proteins, below which edema is likely to develop, is  $5.5 \pm 0.2$  Gm. per cent and for albumin  $2.5 \pm 0.2$  Gm. per cent. Weech and Ling<sup>129</sup> and Lepore<sup>130</sup> found it difficult to produce edema in dogs or human beings with very low plasma protein levels, where a severe sodium ion restriction was effected. Others<sup>131-133</sup> have verified this conclusion, and we have repeatedly confirmed and made use of this fact to prevent or abolish edema formation in hypoproteinemic individuals, where it is difficult or impossible temporarily to restore the plasma proteins because of other considerations. One can hardly sanction the administration of sodium chloride in such liberal quantities as has been advocated, and as may prove necessary, to maintain the plasma chloride level at or above 560 mg. per cent, in the group of patients with low cardiac reserve and/or with uncorrected hypoproteinemia. In our experience this has proved more hazardous than the deliberate development, judiciously tended, of a mild state of dehydration and dechlorination. Usually this can be easily effected by a reduction in the daily supplement of dietary or parenteral sodium chloride. To be sure, since sodium is really the malefactor similar restrictions must be imposed on the use of sodium as the bicarbonate for an antacid or in conjunction with sulfonamide therapy. In the majority of instances with such limitations of chloride and fluid a satisfactory balance is readily struck and future adjustments are made on the basis of the patient's day-to-day weight, plasma chloride level, presence or absence of edema, and related complications. Clinically, such short periods of mild dehydration and dechlorination, carefully supervised, appear to evoke no serious secondary manifestations, while visibly correcting an edematous state and holding it in abeyance until the danger no longer exists of postoperative complications such as impaired wound healing, bronchopneumonia, intestinal stasis, etc.

Scrutiny of the protocols and data of Davis and Whipple<sup>38-41</sup> and Mecray, Barden and Ravdin<sup>116</sup> shows recorded a high frequency of distemper in animals made hypoproteinemic. Whipple stated, "Plasma depleted dogs are even more susceptible to infections (than anemic ones) and many of the dogs used in the earlier experiments died of abscesses, septicemia, endocarditis, and related conditions." The antibody production necessary for opposing infectious processes requires protein in the form of globulin, and is, therefore, influenced by the depreciation occurring in this fraction during many hypoproteinemic states. Such a curtailment would be reflected in a diminished capacity to resist noxious bacterial invasion. The experimental evidence favoring this viewpoint has been discussed by Cannon and associates.<sup>134, 134a</sup> His conclusions afford at least a partial confirmation to the theory since rabbits, after a plasmapheresis depletion of their protein stores, exhibit a definitely decreased capacity to produce antibodies. Also, several other types of small animal experiments designed to test this thesis have yielded confirmatory data.

Other miscellaneous pathologic conditions have been directly or inferentially related to hypoproteinemic states. Hahn and Whipple<sup>135</sup> found that ani-



mals maintained anemic by bleedings produced more hemoglobin when diets contained ample amounts of protein than when they contained low amounts, despite an adequate iron complement in both experiments. Orten and Smith<sup>136</sup> and Orten and Orten<sup>137, 138</sup> found that a mild chronic anemia developed in rats fed a low protein diet, and controls with sufficient protein in the diet had normal blood findings. When the protein content was maintained reduced, but the total number of calories raised, the chronic anemia persisted; increasing the protein content (lactalbumin) with caloric values lowered promptly restored the blood picture to normal. Iron additions to the diet were without effect. Bethell,<sup>139</sup> observing anemias occurring in normal pregnancies, was inclined to believe they were related to an inadequate amount of dietary protein, and noted favorable responses when this component was increased. Studies<sup>74</sup> in progress now at the University of Minnesota Hospitals, upon the obstetrical and gynecological services, rather confirm this impression.

Chang<sup>140</sup> measured the blood volume in patients with low plasma protein values and an associated nutritional deficiency and found these volumes reduced. This has been corroborated in a limited study of our material. This finding has been amply confirmed in experimental animals by Holman, Mahoney, and Whipple,<sup>141</sup> and Elman and Davey.<sup>142</sup> Such a contraction of the total quantity of circulating blood would be likely to exaggerate any shock-producing mechanisms attendant with surgical procedures. De Navasquez<sup>143</sup> described hepatic changes with fatty metamorphosis and brown atrophy of the heart in a case of nutritional edema with hypoproteinemia; Davis and Getzoff<sup>118</sup> consistently demonstrated with the hippuric acid tests, decreased liver function in hypoproteinemic patients.

Less tangible but nonetheless impressive is the characteristic improvement in the patient's general appearance and reaction, amounting almost to a mild euphoria, shortly after conversion from a negative to a positive nitrogen balance. Patients who have been a long time autocannibalistic become indifferent to their needs and surroundings and ultimately incapable even of the efforts required for existence. Others<sup>201</sup> have noted a similar improvement in depleted patients after increasing the nitrogen intake.

In recapitulation, therefore, it can be stated that the causes of hypoproteinemia are legion; the effects of hypoproteinemia are already multiple with many as yet probably unidentified or/but vaguely appreciated. The complexity is heightened, too, by the rather likely consideration that hypoproteinemia arising from one cause may add to its own evil and perpetuation through remote influences, that is, a depression of fabrication in the hepatic substance and anorexia after a local loss from an extensive burn. However, with this knowledge, albeit limited at our disposal, it is now possible to undertake a more rational and less empirical therapy for these major problems of the fatty liver, hepatic dysfunction, and hypoproteinemia.

Starting with the transient supply of proteins with which we are born, and ever thereafter, our bodies require external sources of plant or animal protein for survival. These we eat, digest, absorb, and utilize for energy or refabrication into a specific species protein. Visible dissolution of the ingested

protein begins in the stomach, but under the influence of powerful proteolytic intestinal enzymes this nutrient is fractured eventually into short peptides and amino acids. These, more commonly as the latter than the former, are absorbed into the portal circulation and there serve to provide energy, or to synthesize the bodily proteins of plasma and tissue. All the albumin, fibrinogen, prothrombin, and much of the globulin are formed in the liver from these absorbed products of digested protein. Some globulin is apparently manufactured by the reticulo-endothelial system outside the hepatic substance. Another fraction of the circulating amino acids or more complex aggregates is employed to construct hormones, other protein-containing secretions, and the cellular blood elements. Those amino acids not required intact for these functions are deaminized chiefly by the liver, with the  $\text{NH}_2$  group developing into ammonia which then combines with  $\text{CO}_2$  to form urea. The fatty acid residue when oxidized, then supplies energy directly or if the amino acid precursor was glycine, alanine, arginine, aspartic, serine, cystine, glutamic, hydroxyglutamic, or proline, glucose may be formed and burned or stored as glycogen. The work of discovering which of the twenty odd amino acids were indispensable occupied many of the leading biochemists for years. As a result of the work of all the investigators, Rose<sup>103, 145</sup> was able to present a classification dividing the group into the two categories, essential and nonessential, for growth and maintenance. This work, done in rats, strictly speaking is therefore known to hold only for them, but the best information available now suggests that much the same partitioning is valid for man.

ESSENTIAL	NONESSENTIAL
Arginine	Glycine
Methionine*	Alanine
Isoleucine*	Serine
Leucine	Aspartic
Lysine	Glutamic
Valine*	Proline
Phenylalanine*	Hydroxyproline
Tryptophan*	Tyrosine
Threonine*	Cystine
Histidine†	Hydroxylysine
	Norleucine‡

Since these ten amino acids are essential for normal cellular growth, the quantity in which they are present is probably a limiting factor in plasma protein regeneration. Certain experiments of Madden and Whipple,<sup>146</sup> in which basal diets were augmented with various combinations of essential amino acids, are strongly suggestive.

By means of the process of transamination, that is, the conversion of keto acids  $\text{R-CO-COOH}$  to amino acids  $\text{R-CH(NH}_2\text{)-COOH}$ , within the cell substance certain amino acids are synthesized in the body, thus providing a partial independence in protein fabrication. Unfortunately, all amino acids cannot be

\*The quantities of these amino acids required for promoting growth are greater than for the unstarved group. Absence or severe limitation in amount of any one of these starved acids seriously limits growth.

†This amino acid may not be essential in man.

‡This is included in some lists as essential for growth and maintenance.

lum which is about 13 to 15 per cent protein. Weech<sup>161</sup> has stated that it does possess a "lingering unpleasant taste, difficult to disguise and rendering it rather unpalatable for human consumption." The associated odor is reminiscent of the hot glues used in woodworking and cabinetmaking. With the exception of a product made available to us for experimental purposes, crystalline bovine plasma protein, about 95 per cent protein, we are, therefore, relegated to items of lesser (medium according to the table) potency. Many here can be excluded by objections which appear to be reasonable. All uncooked meat is eliminated for routine use because of the danger of transmitting brucellosis.<sup>166</sup> There seems to be no simple manner of excluding this possibility from uncooked flesh short of pasteurization. Culture methods require too prolonged periods of incubation and are impractical for excluding positively this possibility. The use of cooked kidney yields erratic results (note columns 2 and 3 of Table I). The ingestion of yeast and bran in bulk tend to cause a diarrhea in many individuals. Thyroid powder and liver extract are obviously unsuited for quantity usage. Gizzard, beef muscle, and salmon allow little variety in the menu and the per cent of protein in each gram bulk, is large. The fat content of soy bean meal is too high. Lactalbumin, casein, egg white (ovalbumin and ovaglobulin), polished rice, and powdered Irish potatoes ultimately remain for consideration. We have acquired no experience with the use of the latter two substances. The first three substances are complete proteins (contain all the essential amino acids) and have been the materials used in acquiring much of our biologic information. They are cheap, particularly the casein and lactalbumin, are available in quantity, can be easily added to any one of several dietary dispensing vehicles, and, for the average palate, present no serious degree of gustatory repugnance. The selection of casein and lactalbumin for fortifying diets was favorably influenced also by the apparently high-grade protection of the liver obtained with feeding of this substance in the experiments of Davis and Whipple.\* Skim milk powder was, therefore, selected as the stock material since it fulfilled so many of the requirements. The cost per pound is very reasonable (approximately 20 cents per pound); many billions of pounds are produced annually. In producing skim milk powder, nothing is added to the milk and only the butterfat, water, and much of the vitamin content is removed. The average composition of skim milk powder is as follows:<sup>167</sup>

COMPONENTS	PER CENT
Fat	1.0
Water	3.0
Protein	37.8
Casein circa	32.0
Lactalbumin circa	5.2
Lactoglobulin circa	0.5
Lactose	49.7
Ash	8.5

\*In this connection it seems pertinent to note that casein and lactalbumin have a significantly higher methionine content<sup>34</sup> (3 and 2.8 per cent, respectively) than several other edible proteins. Hen ovalbumin, also an integral part of the diets, probably has the highest methionine content with 5.3 per cent.

The total nitrogen composition of skim milk powder is about 5.4 per cent. Of this total nitrogen, 76 per cent is casein nitrogen, 18 per cent noncasein protein nitrogen, and 6 per cent nonprotein nitrogen. This material\* and a fortifying substance to augment the carbohydrate content were the selections then for diets to be devised which would possess a high protein, carbohydrate, caloric, low fat composition. In developing this theme it seemed wiser to use as vehicles fruit juices,† egg-nogs, purées, and soups, whose nutritional makeup could be augmented with protein and carbohydrate. Lactose was originally chosen to enhance the carbohydrate content since there was evidence in the literature suggesting that it was less liable to induce diarrhea when fed in quantity than were other sugars. This finding has not been confirmed, and it is our impression that this problem is minimal whenever the dispensing apparatus is maintained thoroughly clean or preferably sterilized. An additional aid in avoiding this difficulty is the routine use of some form of appropriate refrigeration for those portions of the diet awaiting dispensing. Should diarrhea develop it can usually be remedied satisfactorily and promptly by rechecking on the techniques involved in the aforementioned precautions, and by the coincidental administration of paregoric in modest amounts. For intervals of several months no single instance of diarrhea will appear, despite a frequent change in personnel among the nursing staff and semiskilled help preparing this material, under the supervision of the dietetic staff. Finally, we have been compelled to abandon the routine use of lactose because of lack of availability of the material, and because its cost was so great compared to beet or cane sugar. Due to the strictures involved in securing sufficient quantities of this carbohydrate we have been substituting "cerelose."‡ It has proved a satisfactory, inexpensive replacement for the cane or beet product, and has the added advantage of being only three-fourths as sweet as sucrose.

The diets with which we have been concerned have been almost exclusively liquid in nature. This has had advantages and disadvantages. Against the idea is the fact that only a relatively meager selection and rather unvaried menu is available. Also, it is a common feeling that no meal is really eaten, certainly not a satisfying one, unless some article can actually be chewed on during the course of the repast. Unfortunately for this frame of mind, clinical experience has shown that the individual's insistence on swallowing a partially masticated bolus of solid material, a piece of beefsteak, for example, presents to the somewhat occluded gastroduodenal aperture a well-nigh insoluble problem in aboral transportation. A short period of time spent in explanation with such individuals, invariably removes this reluctance to co-

\*A variety of more refined commercial preparations have been sampled as alternative means of augmenting the protein and carbohydrate values. These possess certain advantages of increased palatability and solubility, but have been so disproportionately expensive as to discourage their routine use and rather limit the application to special instances.

†A host of carriers has proved satisfactory for this purpose, and a partial list would include orange juice, lemonade, pineapple juice, apple cider, cherry nectar, bananas powdered or homogenized from the whole fruit, grape and grape fruit juice. Substituting freely from this list will alter the over-all content of protein, carbohydrate, and fat very little since the preponderant influence on these nutrients comes from the fortifying substances of milk powder and a sugar.

‡Dextrose from corn processed by the Corn Products Refining Company, St. Paul, Minn.

operate during the temporary all-liquid feeding regimen. The fluid character of the diets has proved advantageous to the dietetic staff. Semi- or unskilled workers readily learn the simple necessary manipulations and mechanics involved in the production of these formulas. On the practical side it was essential that one diet be available for drip feeding through even a small bore nasal tube.

A number of diets have been proposed in the literature for purposes of alimentation via the oral, gastrostomy, or jejunostomy route. In each instance they have not been adapted to this study because of one or more of the following objections:

1. The percentage of fat contained was too high. The inadvisability of this has been mentioned earlier.

2. The protein percentage was too low. Such diets would be automatically excluded.

3. The number of calories per cubic centimeter, described by the neologism, calorie equivalent, is too small. If attention is not devoted to this detail, the bulk of liquid administered becomes excessive as one strives to attain a high caloric feeding schedule. About 1.5 calories per cubic centimeter is desired.

In recapitulation it can be said that the contemplated diet was to possess these characteristics: It would be a high protein, carbohydrate, low fat diet with a high caloric equivalent; its production would be simple, relatively inexpensive, and in a form readily tolerable, in appearance and taste to the patient—and to his intestinal tract. No emphasis was to be placed on the vitamin content of the diet and it was decided to rely on the routine administration of such quantities of vitamin B<sub>1</sub> (thiamine), B complex (crude liver extract), C (ascorbic acid), and K as appeared indicated in each individual case. The minerals, calcium, phosphorus, and iron have been estimated to be present in satisfactory quantities when a single portion of Diet I or II is consumed.

This information was secured chiefly from charts in Bowes and Church<sup>23</sup> and the values listed here have been reduced to close approximations.

	DIET I (ONE PORTION)	DIET II (1,500 C.C.)
Calcium	5.2 Gm.	2.8 Gm.
Phosphorus	4.2 Gm.	2.6 Gm.
Iron	19.0 mg.	16.0 gm.

These amounts listed exceed, when but a single portion of either diet is consumed, the daily allowances recommended in the *Handbook of Nutrition* for 1943.

#### DESCRIPTION OF PROPOSED DIETS

For the preoperative dietary management of surgical patients, Diets I, II, IIA, III, and IV have been developed. In each the goal was to adhere as closely as possible to the previously listed qualities and characteristics. Specific differences, within these limitations, were "built into" each diet. Diet I is designed to be quite reasonably palatable, with a wider range of vehicles, and

## DIET I

		Calories	2,426.00			
		Protein	160.20 Gm.			
		Fat	18.05 Gm.			
		Carbohydrates	407.00 Gm.			
		Caloric equivalent	1.60			
		VOLUME OR WEIGHT	P.	F.	CHO	CALORIES
7 A.M.	1/4 cup oatmeal, strained	10 Gm.	1.4	0.75	6.8	40
	3/4 cup skimmed milk	180 c.c.	6.3	0.40	9.0	65
	2 tbs. lactose*	30 Gm.			30.0	120
9 A.M.	1 cup orange juice	240 c.c.			24.0	96
	1 tbs. lactose	15 Gm.			15.0	60
10 A.M.	Skimmed milk powder	120 Gm.	40.4	1.20	58.8	408
	1 cup skimmed milk, warm	240 c.c.	8.4	0.50	12.0	86
	1/2 cup puréed peas	50 Gm.	3.3	0.20	10.1	55
12 M.	1 cup orange juice	240 c.c.			24.0	96
	1 tbs. lactose	15 Gm.			15.0	60
2 P.M.	Eggnog:					
	1 egg	Variable	6.4	5.80	0.4	79
	Skimmed milk powder	30 Gm.	10.1	0.30	14.7	102
	1 tbs. lactose	15 Gm.			15.0	60
	1 cup skimmed milk	240 c.c.	8.4	0.50	12.0	86
4 P.M.	Skimmed milk powder	120 Gm.	40.4	1.20	58.8	408
	1 cup skimmed milk, warm	240 c.c.	8.4	0.50	12.0	86
	1/4 cup puréed beans, string (fresh, frozen, or canned)	50 Gm.	1.0	0.10	3.3	18
6 P.M.	1 glass grape juice	240 c.c.	0.8		44.0	179
8 P.M.	Eggnog, same as 2 P.M. feeding	about	24.9	6.60	42.1	327
Totals		1,500 c.c.	160.2	18.05	407.0	2,431

\*Beet, cane sugar, or cerelese can be substituted.

to be presented to the patient in divided portions every few hours during the daytime. In Diet II, with a high caloric equivalent, the emphasis is less on tastiness, yet it should be palatable, and more on securing a freely flowing mixture, to facilitate feedings via a nasal tube. Diet IIA consists of 1,000 c.c. of Diet II to which has been added the filtered residue remaining from one pound of ground raw liver after homogenization in a Waring blender. This machine effects nicely the breakdown of liver parenchyma into finely divided particles capable of passing easily through a nasal tube when they are suspended in Diet II as the vehicle. The fibrous connective tissue elements resist

## DIET II

		Carbohydrates	408.8 Gm.			
		Protein	120.4 Gm.			
		Fat	37.2 Gm.			
		Calories	2,446.0			
		Volume	about 1,500.0 c.c.			
		Caloric equivalent	about 1.6			
		CHO	P.	F.		
6 whole eggs			36.0		36.0	
2 egg whites			8.0			
4 oz. skimmed milk powder	58.8		40.4		1.2	
300 Gm. lactose*	300.0					
1,000 Gm. skim milk	50.0		36.0			
5 gr. salt (may be added when indicated)	408.8		120.4		37.2	

\*Beet, cane sugar, or cerelese can be substituted.

large quantities, may influence the total amount of substance ultimately to be stored in body depots. Also, occult edema, which could represent as much as 5 to 6 per cent of the total body weight might be present but undetected. The simultaneous substitution with bodily tissue and disappearance of this amount of fluid by virtue of the improved nutrition is a tentative possible alternative explanation. Finally, any conversion of protein or carbohydrate to fat would require an intake to storage ratio of more than two to one. In order to exclude the rather unlikely possibility of a failure of intestinal absorption of protein and carbohydrate, samples from four-day stool specimens were analyzed. These determinations uniformly indicated excellent absorption of the protein component despite an intake of as much as 500 Gm. daily. Consistently, there was less than 10 per cent of the ingested protein in the stool.

Cases 3 and 4 represent rather typical examples of this type of feeding plan.

CASE 3 (No. 741769).—A. W., aged 59 years, reported that for fifteen months prior to admission there had been epigastric postprandial distress associated with nausea, vomiting, and a developing weakness. Emesis had increased gradually in frequency. Weight loss had been steady and more marked recently, so at the time of admission the weight loss was 30 per cent. No obstruction was noted in a gastrointestinal series of roentgenograms interpreted as showing a large gastric ulcer. During the following twenty-one days this patient received an average of 6,000 calories daily, from Diets I and II ad libitum. The patient displayed no diarrhea nor glycosuria, and had no gastric retention or emesis. This represented an intake of more than 7,200 Gm. of protein or nearly 350 Gm. daily. One transfusion of 350 c.c. of blood was given. No dehydration or edema was present on admission, nor did any develop during this period. The hemoglobin, red blood cell, and plasma protein values are listed below:

DATE	3/29/44	4/18/44 (DIETARY PREPA- RATION STARTED)	4/24/44	4/28/44	5/1/44	5/6/44	5/8/44 (DAY OF SUR- GERY)
Hemoglobin (Gm. %)	9.45	8.46	11.8		10.3		
R.B.C. (millions per c.mm.)		2.55			3.26		
Plasma proteins (Gm. %)	3.72	5.7		5.6	6.2	5.4	

It is not too difficult to explain how such large amounts of protein in the diet seemingly fail to evoke by this means a consistent detectable increase in the plasma protein values. This is, I believe, a clear manifestation of how unsatisfying may be the information secured through determinations of the plasma protein value. Often, small changes in these values appear to be associated with quantitatively much larger alterations in the plasma volume and the labile protein stores or components of bodily tissues; for these three quantities, albeit regulated by a host of external and internal factors, appear to remain in equilibrium. Considered somewhat differently they represent the three geometric dimensions required for the definition of volume. The first two of these determinations, plasma proteins and plasma volume, usually can be secured readily, but the final dimension, the tissue component, seems at this writing least susceptible of mensuration. When, however, a clear-cut rise or fall in the plasma protein value is noted, judgments as to the state of nitrogen balance can be

offered with more assurance of their accuracy. Yet, even here, the incompleteness of these observations hovers like a discouraging shadow over any illuminating discussion of the problem. It seems logical to infer that one of the mechanisms producing the hypoproteinemia originally could be capable of maintaining this status quo, despite the provision for ample sources of protein for regeneration. Subjectively this patient was much improved and appeared adequately prepared nutritionally for surgery. No detectable evidence of hepatic dysfunction existed. The postoperative convalescence was prompt and complicationless.

CASE 4 (No. 732161).—C. B., aged 68 years, had noticed epigastric distress of a mild sort for two years before admission. For the last year there had been anorexia and a progressive weight loss which at the time of admission equaled thirty-five pounds, about 27 per cent of the usual body weight. The local physician had informed her that she was anemic and had a tumor of the stomach. These diagnoses were confirmed, and x-ray studies secured in this clinic revealed a massive carcinoma involving the distal two-thirds of the stomach. These pictures corresponded well with the size of an easily palpable epigastric mass. Gastric retention was not present. Three transfusions adjusted the hemoglobin satisfactorily. This patient averaged in excess of 6,000 calories daily for thirteen days from Diets I and II, without demonstrable weight gain. After this preparation she was operated upon and about a 96 to 98 per cent gastric resection completed. Convalescence was uneventful and the patient was discharged on the twelfth postoperative day.

*Cases Exhibiting Pyloric Obstruction, But Less Than Complete in Degree.*—Patients with partial obstruction are given limited quantities of Diet I by day and Diet II by night. From midnight to 8:00 A.M., during the initial days of this feeding schedule, no more feeding is allowed. The stomach is then evacuated by nasal tube and the quantity removed is accurately measured and recorded. Patients having aspirations of less than 300 to 500 c.c. are continued upon this regimen with a limited intake when the calorie intake approximates or exceeds 3,500 calories daily. For example, if the intake consisted of one portion of Diets I and II with 500 c.c. being aspirated, the total effectual nutrient intake would substantially surpass the minimum requirement of 3,500 calories. Those patients, in this category, with high-grade but not complete pyloric obstruction, in whom the retention is more voluminous, are cared for in the following fashion: A nine-hole nasal tube is inserted into the stomach and the Diet II mixture allowed to trickle at a very slow rate, drop by drop, through a Murphy drip set. A demonstration of this setup is portrayed in Fig. 5.

For this purpose it has proved advantageous to use intravenous flasks\* so constructed that air rises through the contents in the container while the liquid flows from another dependent aperture. This bubbling effect provides enough mild agitation to prevent much of the aggravating tendency for plugging which occurred when certain other types of dispensers were employed. The average patient readily cooperates in regulating the flow rate by adjusting, from time to time, a thumbscrew clamp fastened distal to the Murphy drip bulb, which serves as a visible and reliable guide during waking hours. Maintenance of such equipment in smooth working order is but another of the many burdens a tolerant nursing staff discharges so faithfully with but scant recog-

\*Manufactured by The Upjohn Company, Kalamazoo, Mich.



niton. Occasionally the prolonged presence of an indwelling nasal tube brings about real torment through local irritation. Two devices have been tried, with the second the more satisfactory in our experience. Woldman<sup>168</sup> suggested the use of a collapsible indwelling nasal tube. This device closely resembles Penrose tubing about  $\frac{1}{4}$  inch in width with a spiral strand of silkworm gut threaded down the middle to serve as an obturator. This facilitates passage of the tube into the gastric area. In the absence of the manufactured article, ordinary narrow Penrose tubing can be passed, with the aid of a catheter, through the nose and out the mouth. Then a large size gelatin capsule can be tied to a short catgut leader fixed to the aboral end of the tube. When this bolus is swallowed



Fig 5.—Drip feeding apparatus.

with a gulp of liquid or spoonful of mashed potatoes, the tubing is readily led along down the esophagus. The soft compressible rubber cylinder is readily tolerated by individuals aggravated by a stiffer conduit. It does have an annoying inclination, because of this excessive flexibility, to kink and thus plug, with changes in head posture by the patient. The alternative device has been the use of a vinylite resin (vinyl acetate) tube, of small bore. This material is smooth, pliant, and lightweight. It glides easily over mucous membranes and evokes little adverse criticism. The lack of an abundant supply plus a tendency to deterioration after prolonged exposure to gastric acids has limited its application to the more sensitive individuals. It has seemed to be a useful and satisfactory expedient.

As ancillary measures in the treatment of this type of case, we have routinely administered atropine sulfate, gr.  $\frac{1}{150}$ , and sodium phenobarbital, gr. 1 to 2 hypodermically, every four to six hours. Mears<sup>169</sup> has pointed out that therapeutic doses of atropine sulfate, hypodermically, every few hours materially reduces the quantity of gastric juice secreted; Merendino and Litow<sup>170</sup> noted a similar, although less marked, depression on the flow of gastric juice when sodium phenobarbital was injected periodically subcutaneously. In addition, the sodium phenobarbital aids in controlling the motor restlessness and irritability often encountered in such cases where ulcer is the underlying mechanism. Also, it allays in a large measure the discomfort from an ordinary nasal tube. These various adjuvants, we feel, reduce the total bulk of fluid seeking outlet through a gastroduodenal opening reduced in lumen and thereby contribute to an adjustment to tolerable limits, the task of a decompensated stomach.

An additional physiologic consideration is worthy of discussion at this time. In certain instances patients being treated by the Sippy regimen were noted to exhibit large volumes of gastric retention unvaryingly day after day. Then, after the employment of the intragastric drip feeding routine with Diet II, the retention frequently decreased significantly in amount and not infrequently disappeared completely. This phenomenon, it is granted, is open to alternative explanations, yet it provides interesting material for speculation. To prescribe the Sippy regimen is to prescribe a high fat type of feeding. One of the most clearly established physiologic responses noted after a fatty meal is an inhibition of gastric motility.<sup>171-175</sup> This depression of peristaltic activity conceivably depresses gastric evacuation and, under such circumstances, is therefore not acceptable. Also, in the Sippy method of treating ulcers, the patient customarily gulps a two or three ounce mixture approximately every hour or so. The swallow carries down with it a complement of air and then this quantity is presented before the narrowed pyloroduodenal exit. In our experience, the stomach more efficiently evacuates its contents when called upon to handle a cubic centimeter every minute than when it must adjust for a 60-90 c.c. load, all at once, repeated hourly.

A patient treated in this fashion is reported in Case 5. The stability of the blood pressure and pulse rate and the smooth brief period required for convalescence seem significant in this man with a serious weight loss.

CASE 5 (No. 728192).—W. W., aged 61 years, had chronic epigastric distress and anorexia for the three years prior to admission. During the final three months of this period these symptoms had increased in severity and there was an associated nausea, vomiting, and ease of fatigability. During this latter interval, he had lost thirty-four pounds in weight, a 30 per cent weight loss. The x-ray examination of the stomach indicated a "marked retention of barium and findings which would be most consistent with an ulcerating carcinoma of the antrum." During a four-week period, preparation was secured largely with intragastric feedings of Diet II supplemented with plasma transfusions and 20 per cent glucose intravenously. This preparation was complicated, prolonged, and made less satisfactory by periodic episodes of almost complete gastric retention which would spontaneously clear up with continuation of the same therapy under which they had developed. There was a 1.5 kilogram weight increase and the plasma proteins fell from 7.5 to 6.7 Gm. per cent during the period of preparation. At the conclusion of this preparation

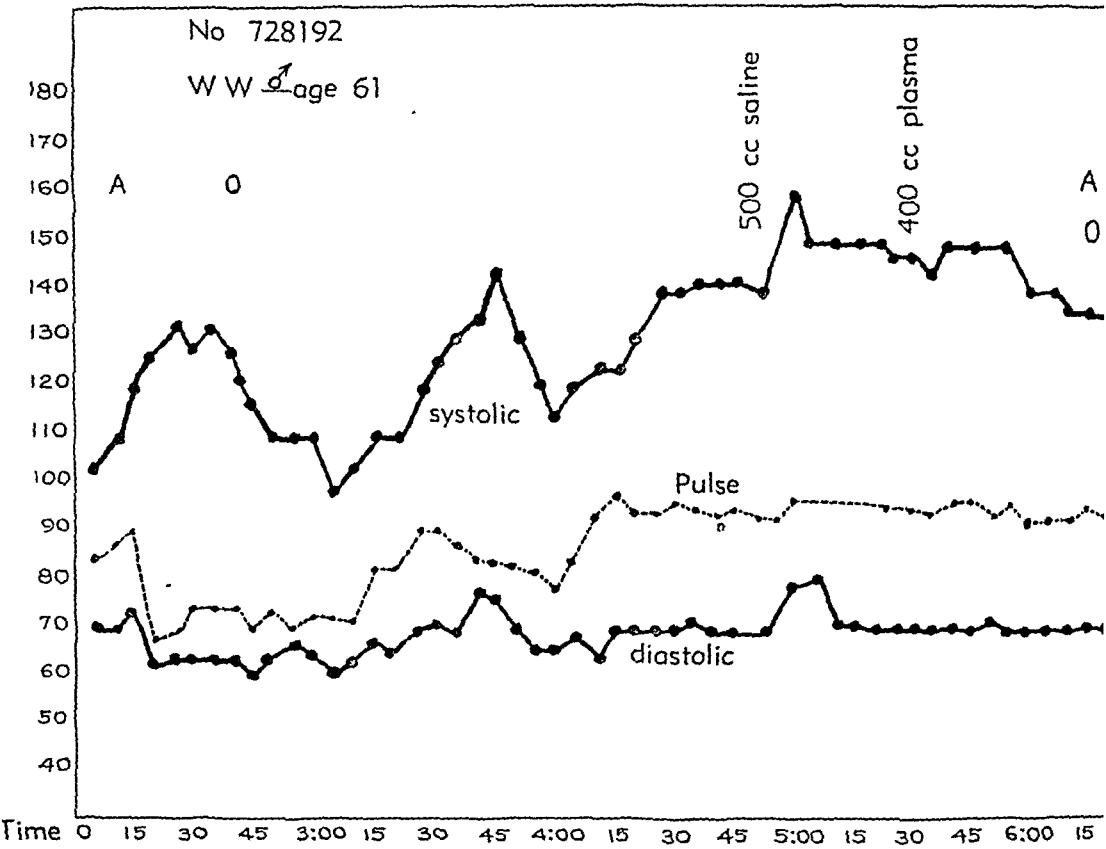


Fig. 6.—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 5).

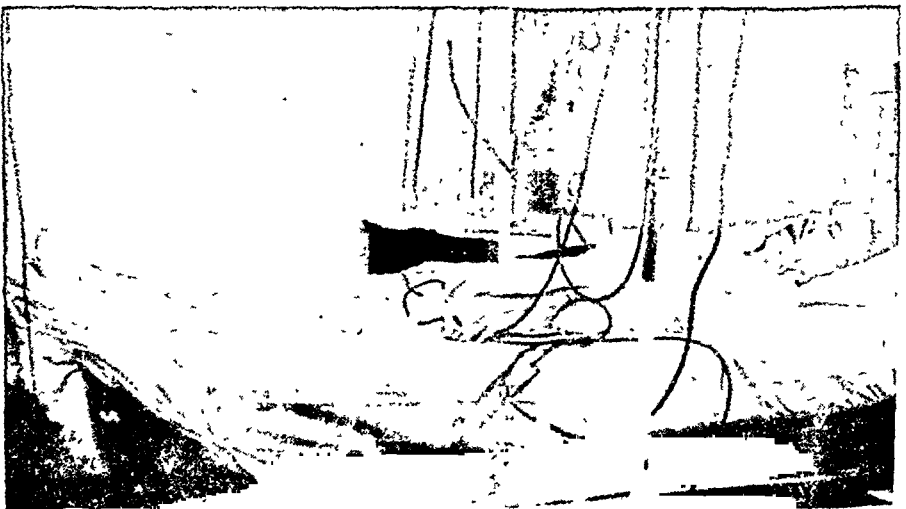


Fig. 7.—Photograph of patient during preparation (Case 5).

a subtotal gastric resection was performed and convalescence was uneventful, with the patient leaving the hospital on the fourteenth postoperative day. This patient has remained well during the past one and one-half years since surgery and returned to a more normal weight.

*Cases With Complete Pyloric Obstruction.*—In instances of complete obstruction, two alternatives are present. A jejunostomy can be made for feeding purposes, and the surgery of magnitude performed when an adequate nutritional state has been restored. We have had virtually no experience with such a plan. Apparently, however, even such a minor procedure can be associated with the development of a temporary but rather intractable state of negative nitrogen balance. Cuthbertson<sup>225-227</sup> first called attention to the increased rate of nitrogen elimination in the urine after injuries (fractures), found the imbalance rose sharply in the three days after trauma, and persisted for several more days, despite, and almost uninfluenced by, substantial augmentation of both the caloric and nitrogen intake. Howard and his associates<sup>229, 230</sup> have corroborated these observations and have protracted the investigation while noting the maintenance of a negative nitrogen balance for more than one month in certain fracture cases. In the simpler operative procedures the nitrogen loss is as real but shorter in duration and quantitatively smaller. Peters<sup>231</sup> reported that a similar situation occurs in the acute infectious processes studied, with a daily nitrogen deficit persisting after subsidence of the acute aspects of the disease, despite an intake of 178 Gm. of protein per day. This seemingly, anomalous transitory failure of the bodily mechanisms to anabolize available amino acid elements has been interpreted by Albright<sup>232</sup> as an expression of Selye's "alarm reaction" engendered by an abnormal secretion of adrenal cortical hormone "S." The solution to this particular conundrum of biology may well involve mechanisms more intricate than this, however, for Munro and Cuthbertson<sup>228</sup> noted the absence of any real antianabolic period when rats were deprived of protein for a sufficiently long period prior to a fracture injury. Also, Co Tui and collaborators<sup>233</sup> were able to develop a strongly positive nitrogen balance in patients submitted to major surgical procedures when about 200 Gm. of protein (the powdered enzymatic digest of casein and pork pancreas, Amigen) was ingested daily beginning in the early phases of postoperative recovery. Elman and associates,<sup>179</sup> too, approximated these results postoperatively utilizing the same source of protein. Within the scope of our present knowledge it is difficult to resolve these apparent contradictions between the groups of investigators. However, the impression is created that whenever feasible the ingestion of protein as an aspect of preoperative preparation is as effective as, or more effective than, corresponding increments made available to the patient in the post-traumatic interval.

The other choice is to supply the patients nutritional needs largely or completely by the intravenous, subcutaneous, or sternal routes as best one can, and this is often accomplished with modest effectiveness. Periodically, reasonable quantities of Diet II are supplied and then followed by a fasting interval. The gastric aspiration at that time is checked for any relenting in the obstruc-

tive element. The caloric intake is thereby complemented somewhat. The bulk of the daily caloric intake is provided, nevertheless, by hypertonic glucose solutions, preferably 20 per cent in distilled water, dripped intravenously at the rate of 100 to 125 c.c. per hour through a fine caliber (No. 20 or 22 gauge) needle. It should require ten to twelve hours for 1,500 c.c. (yielding 1,200 calories) to be injected. Hourly rates in excess of this encourage glycosuria with subsequent loss of greater amounts of the nutrient and a concomitant undesirable dehydration effect. When it is injected at this suggested pace, which exceeds somewhat the prescribed "desirable rate of infusion,"<sup>224</sup> the total spillage in the twenty-four hour urine collection in our experience has been consistently less than 1 per cent. Insulin is not added to the solution in the normal subject, and evidence of the beneficial effects of its use under such condition is controversial.<sup>176-178</sup> The use of a cubital vein with the arm hyperextended in the routine manner for intravenous therapy is to be avoided because of several considerations. This position is acutely distressing for anyone to maintain longer than a short while. Consequently, the patient tries to relieve the discomfort by some degree of flexion at the elbow, readily and frequently plunging the needle through the back wall of the vein and leading to a paravenous infusion. With strongly hypertonic solutions this is a particularly undesirable complication, and, at best, results in a locally tender, inflamed sore arm. Another reason to avoid this site is related to the frequent occurrence of thromboses in veins carrying hypertonic glucose solutions. If the broader channels are occluded early in the course of a prolonged feeding schedule, the difficulty of the task is enhanced and these areas are no longer readily available for any emergency infusions of blood or plasma that may be required during the operations or the convalescence. The preference has been, therefore, to insert the needle into a forearm vein, away from the cubital fossa, and in such a position as to allow the arm a free range of motion (see Fig. 8).

No arm board is required. A feeling of assurance is imparted the patient by splinting the forearm slightly with a few thicknesses of newspaper or cardboard encircling the area and fixed in place by a strip of bandage. The caloric intake is further supplemented by the subcutaneous administration of at least 1,000 c.c. of 5 to 10 per cent glucose in distilled water or saline solution as determined by the electrolyte need and hydration of the patient. A positive nitrogen balance is strived for by two means. Protein is provided by the daily intravenous administration of liberal amounts of plasma. Nitrogen equilibrium in dogs<sup>142, 149, 156, 180, 181</sup> and man<sup>182</sup> can be maintained for many days in this fashion, excellent evidence that such parenterally administered protein is metabolized. It is soon noted under such conditions that surprisingly larger quantities of plasma must be infused than one would calculate from the theoretical plasma volume, to elevate appreciably the plasma protein value. Since protein so injected does not cause a disproportionate rise in urinary nitrogen, this is then explicable as another manifestation of the extremely fluid equilibrium which exists between plasma protein and other protein stores. The conclusion is equally reasonable that small deficits in the former mirror quanti-

tatively gross debits in the latter. Earlier workers<sup>148, 160, 163</sup> noted that of the total nitrogen lost during fasting, only a small fraction could be accounted for on the basis of the albumin lost from plasma protein. Sachar, Horwitz, and Elman<sup>183</sup> studied the problem in some detail in dogs and arrived at a ratio of 25 to 30:1 for the respective contributions of albumin and tissue protein to total amount lost during a fast. The evidence<sup>181</sup> on the same subject for man is meager but in general agreement with the ratio revised toward 30 to 40:1. A few simple calculations may serve to clarify this point. If, in a 60 kilogram man, the plasma protein value has been lowered by starvation from the normal average 7.5 to 6.5, this represents but 30 Gm. of protein lost from the plasma volume of this individual.\* Granted the tissue-plasma protein ratio of at least



Fig. 8.—Suggested position of needle for prolonged intravenous therapy.

30:1 exists, then 900 Gm. of tissue protein have also been lost. To replace this, therefore, about 12,400 c.c. of plasma with total proteins of 7.5 Gm. per cent are required. The total eventually necessary, however, surpasses even this figure, since such an amount cannot be given intravenously within even a few days. During this interval additional protein is being catabolized which needs to be replaced by more plasma. A good deal less than complete replacement therapy is, therefore, the only goal actually attainable. The surgeon should appreciate the difficulty of restoring intravenously completely the body protein depots, aim at preventing additional depletion of existing protein stores, and, if possible, establish a nitrogen balance as favorable as possible. Fortunately in this situation there is a true equilibrium, and in the situation where ample stores exist, the protein reservoirs are capable of replacing 40 to 60 per

\* (Aver. plasma prot.  $\frac{7.5}{6.5}$  - reduced value)  $\times$  (Wt. in kg)  $\times$  ( $\frac{100}{.05}$  total body wt. in plasma)  
 $\times 10 = 30$  Gm. protein

cent of the total circulating plasma proteins in twelve hours after a sudden severe loss. Over a longer interval with repeated demands, these depots may supply an amount of protein equal to 200 to 300 per cent of the original total circulating plasma protein. This mechanism appears to function in man<sup>185</sup> at a reduced rate if the protein depletion has been associated with the production of shock.<sup>186</sup>

A portion of the nitrogen requirements can be provided through the agency of intravenously injected amino acids, usually obtained from the enzymatic or acid hydrolysis of casein. The resulting mixture in the latter instance is poor in tryptophane and probably also the sulfur-containing amino acids and these essential amino acids must, therefore, be replaced if the solution is to be effective in protein regeneration. After the original experiments of Lowe<sup>187</sup> in 1901 had demonstrated that, by feeding protein digests nitrogen equilibrium could be attained, observations on parenteral alimentation with such amino acid preparations were for many years sporadic. Abderhalden, Frank, and Schittenhelm<sup>188</sup> and Abderhalden<sup>189</sup> tried rectal administration and found evidence of absorption and utilization. This has been confirmed since.<sup>190</sup> Henriques and Andersen<sup>191</sup> kept a goat in positive nitrogen balance for one month with intravenous injections of meat digests. To Elman belongs the credit for reviving and stimulating interest in this problem. Much of our present knowledge and success the method now enjoys is related to the efforts of him and his associates.<sup>192-198</sup> They have demonstrated the necessity of having mixtures containing all the essential amino acids, if retention and protein synthesis is to be accomplished. In dogs a positive nitrogen balance has been effected with intravenous injections of amino acids as the sole source of protein. It has even been possible to induce some degree of plasma regeneration under these conditions<sup>200</sup> or when the ten essential amino acids (Rose) are provided in pure crystalline form.<sup>199</sup> Investigators<sup>201-204</sup> have had difficulty in acquiring unequivocal evidence that plasma protein regeneration can be realized in adults by the infusion of amino acids as the sole source of protein. Mueller, Fickas, and Cox<sup>205</sup> using an enzymatic hydrolysate of casein, 85 per cent, and pork pancreas, 15 per cent, found that 0.7 Gm. per kilogram with an otherwise adequate caloric intake was hardly enough to keep a positive nitrogen balance for a four-day period. Studies at this clinic suggest that quantitative as well as qualitative differences may arise when viewing the oral versus the intravenous routes for protein uptake by the body. The quantitative boundaries are rather sharply limned since it requires about fifteen to twenty hours of each twenty-four to drip in the 6,000 c.c. of 5 per cent\* amigen solution necessary to provide the nitrogen content equivalent to 225† Gm. of protein. When injected at rates faster or with an increased concentration there is a greater tendency toward unpleasant systemic manifestations. Additional limitations exist. The bulk of fluid necessary as a vehicle for such a quantity of amigen

\*This solution is usually made up with a 5 to 10 per cent concentration of glucose.

†Dietary intakes far in excess of this are readily assimilable.

looms large to anyone, but to the patient with a low cardiac reserve it may be insurmountable when reinforced by a sodium content in the amigen solution of such an order of magnitude as to constitute a real problem per se. For the seriously hypoproteinemic individual such hazards appear to be quite as genuine. Qualitative differences are somewhat less clearly definable, yet do seem to obtain. For instance, in a number of our experiments the total nitrogen content of the twenty-four hour urine collection secured after supplying 2,000 to 6,000 c.c. of 5 per cent\* amigen solution intravenously (as a slow drip infusion) has been higher than daily total urinary nitrogen values obtained while feeding equivalent quantities of skim milk powder or bovine plasma protein. No broad indictment against nitrogen replacement by intravenous preparations is implied, for no one can gainsay that it has an important role in such therapy. However, since knowledge of the limitations involved, when parenteral clysis is the sole feeding route, seem to be less generally recognized and heeded, this brief discussion appears germane. It is apparent, therefore, that large quantities of intravenous fluids must be injected to introduce enough amino acids for both maintenance of nitrogen equilibrium and promotion of plasma protein regeneration. Any real protein need or other mechanisms for depletion besides inanition, that is, infectious processes, purulent exudates, or ulceration, would promptly and materially increase the requirements necessary for plasma protein regeneration. Without actually achieving this ideal, however, the benefits which can be developed are real and very worth while. Amino acids alone or, preferably, supplemented with daily doses of plasma (or blood when indicated) make it possible to relieve the steady drain that starvation states and the so often associated depleting mechanisms place on the body's protein stores. This interruption of the patient's autocannibalistic tendencies and a measure of restitution by provision for a liver with improved function, low lipid content, and high glycogen values, both increases an individual's chance to negotiate the hazards of surgical intervention and hastens his convalescence. Such cases of complete obstruction, requiring the outlined therapy, are fortunately in the minority, for they require an inordinate expenditure of patience and time during the tedium of maintaining a prolonged intravenous feeding schedule. It is to be emphasized that in these instances of complete pyloric occlusion the surgeon must speed the preparation. Even in those patients with a high-grade weight loss, therapy should be compressed into a period of ten to fourteen days, for these individuals are most prone to develop pneumonia as a complication of regurgitation, inlying nasal tubes, hypoproteinemia, or mere partial immobilization for long periods during intravenous therapy. Despite these obvious handicaps imposed upon the individual seeking an adequate surgical preparation through parenteral feedings, it is usually possible to culminate the issue successfully by the proper care—and good fortune.

Cases 6 and 7, the patients cared for in the main according to this method, are reported here.



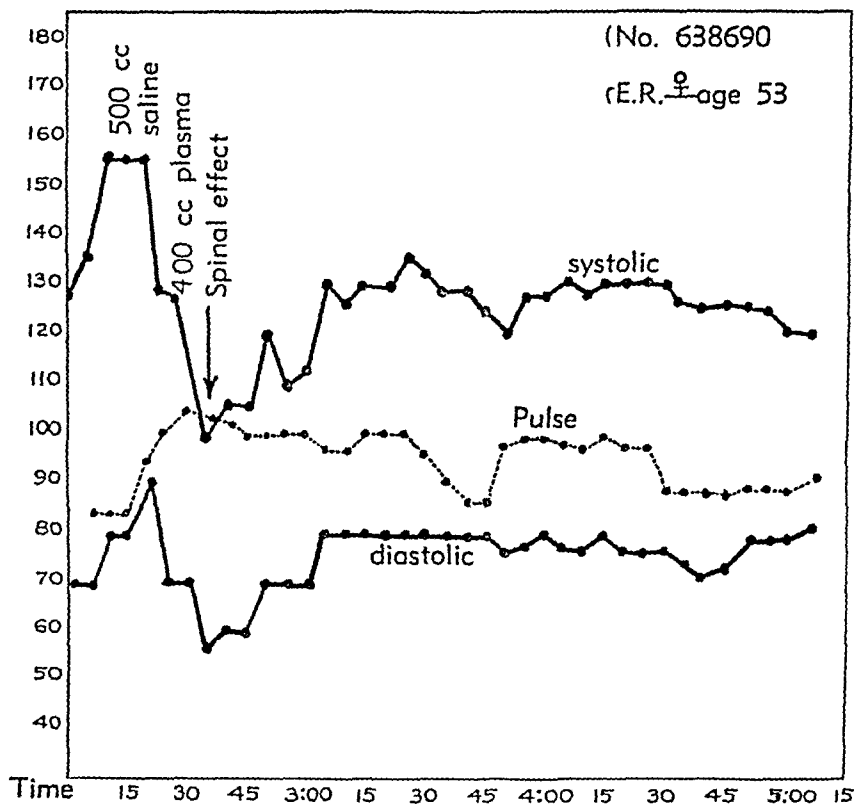


Fig. 9.—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 6).



Fig. 10—Photographs of patient (Case 6); A, secured ten days postoperative; B, secured three months postoperative.

CASE 6 (No. 638690).—E. R., aged 53 years, for the previous thirteen or fourteen years had had a vague sort of epigastric distress, worse after large meals, relieved by soda, adherence to a bland diet, or vomiting (rarely). Repeated barium meal studies of the stomach and duodenum failed to show any ulcer. During the three weeks prior to admission her vomiting had increased in frequency and followed eating in almost every instance. The weight loss represented 35 per cent of the usual heft and the total body weight was sixty-three pounds. She was unable to walk, talk, sit upright, or feed herself. X-ray pictures secured at this time indicated a very high-grade obstruction at the pyloroduodenal outlet. No commitment as to the exact nature of the lesion could be safely made. During a three-week preparation period the degree of gastric retention varied somewhat from day to day, but in general remained vexatiously high. The dietary preparation, therefore, was achieved, in the main, through intravenous feedings of 20 per cent glucose, amino acids, plasma (or blood), and subcutaneous glucose infusions, daily. About 1,000 c.c. daily of Diet II successfully negotiated the stenotic barrier. The weight gain during this period averaged 1.5 kilograms per week. A subtotal gastric resection was then performed and the obstruction noted to arise from contraction secondary to a benign gastric ulcer. Convalescence was uncomplicated and the patient was discharged on the twelfth postoperative day. This patient gained weight, as can be noted in the follow-up photograph secured several months after the operation, and was in good health until the development of a psychiatric disorder about one year later.

CASE 7 (No. 725261).—A. B., aged 78 years, in the six months prior to admission had had anorexia, vomiting, and about a sixty-pound weight loss, representing 37 per cent of the body weight. When seen at the time of admission she could neither sit, stand, talk, nor feed herself. Every breath was an effort and death appeared imminent. Obstruction was present at the pyloric outlet, but it was possible by combining virtually continuous intragastric drip feedings of Diet II, with 20 per cent glucose, amino acids, and plasma intravenously to achieve a daily intake in excess of 4,000 calories. This schedule was maintained for three weeks with little gain in weight. At that time an 80 per cent resection of the stomach for carcinoma was performed. This procedure was readily tolerated by the patient and she was discharged on the sixteenth postoperative day.

#### *Those Cases With Bleeding.—*

*Cases Without Obstruction:* Patients with bleeding but without obstruction are fed continuously twenty-four hours a day with an intragastric drip of Diet II. Objections have been raised of almost a hypothetical nature, inferring that the presence of a soft rubber catheter may provoke additional hemorrhage by prodding the clot from an eroded but temporarily sealed blood vessel. This conjectured aversion seems more chimerical than real. The presence of a nasal tube provides a feeding schedule every minute, every hour, twenty-four hours a day. This appears to be of extreme importance, for two reasons. First, by bathing the gastric mucosa with a protein mixture the resultant pH of the gastric contents is buffered to values where the acid and peptic effects are appreciably reduced. The following representative figures have been secured. In vitro 100 c.c. of 0.1 NHCL is buffered to pH 3 by 160 c.c. of Diet II and to pH 4 by 225 c.c. In another group of tests after a fasting gastric specimen was secured, dogs were given 0.5 mg. of histamine diphosphate subcutaneously. Samples were then withdrawn every thirty minutes, measured for volume, tested for free acid by titration with 0.1 normal sodium hydroxide using Töpfer's reagent as the end-point indicator and for



Fig 11—Photographs of patient (Case 7). A, Secured ten days postoperative; B, secured three months postoperative.

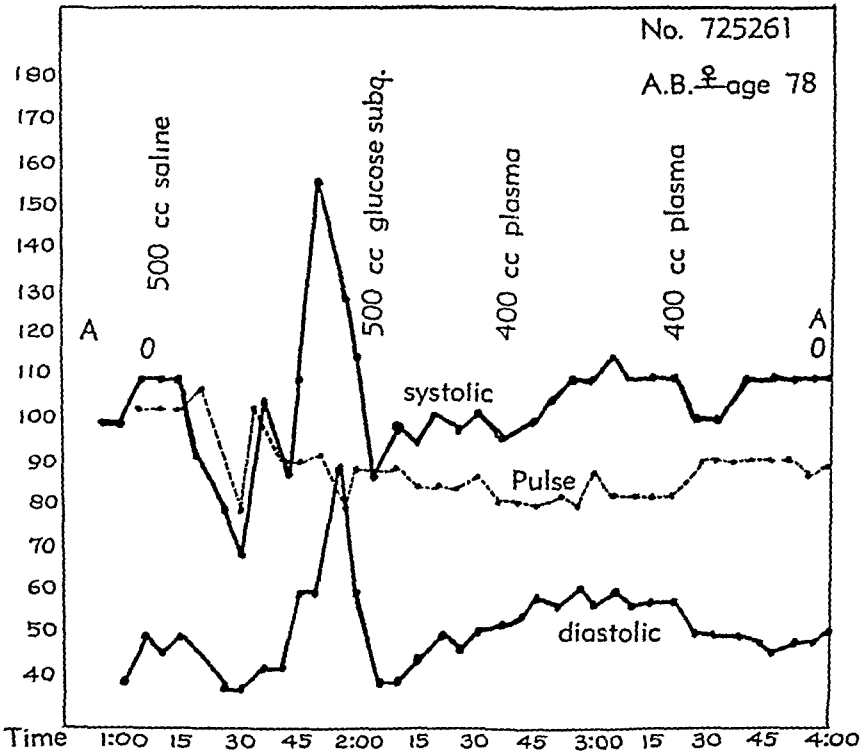


Fig. 12—Record of blood pressure, pulse, and intravenous fluids during anesthesia. Note stable blood pressure and pulse rate after initial early anesthesia effects (Case 7)

total acid with phenolphthalein as the indicator. Hydrogen ion concentration values were secured with a glass electrode in a Coleman electrometer. When the magnitude of this standard stimulus had been recorded in several animals, the procedure was repeated and 400 c.c. of Diet II were instilled, after securing the fasting sample, and at the moment 0.5 mg. of histamine diphosphate was injected. Each time subsequent samples were removed, several aspirations and flushings were performed as a precaution taken to insure that each aliquot removed was representative.

Two typical experiments are charted here.

Dog 164. STANDARDIZING TEST

SAMPLE	DEGREES FREE ACID	DEGREES TOTAL ACID	VOLUME C.C.	PH
1	0	16	4.7	6.01
2	110	118	35.0	1.26
3	127	136	24.5	1.20
4	14	28	1.5	3.51
<i>After Instillation 400 c.c. Diet II</i>				
1	0	12	1.8	5.92
2	0	118	15.0	4.24
3	0	117	51.0	4.39
4	0	90	32.0	3.57
5	0	114	24.0	4.45

Dog 165. STANDARDIZING TEST

SAMPLE	DEGREES FREE ACID	DEGREES TOTAL ACID	VOLUME C.C.	PH
1	0	20	4.6	7.51
2	79	94	48.0	1.46
3	106	118	9.0	1.30
4	72	83	21.0	1.48
<i>After Instillation 400 c.c. Diet II</i>				
1	0	7	3.3	6.54
2	0	148	32.5	5.24
3	0	137	34.0	4.53
4	0	116	30.0	4.07
5	0	129	28.0	4.95

In this pH range nearly all the acid and 80 to 90 per cent of the peptic proteolytic activity have been controlled. Under such circumstances an initiation of the healing processes is conceivable. Clinical experience has shown that in the absence of obstruction and in the age group under 45 years a gratifying number of operations for bleeding ulcer can be deferred (days if necessary) until the judgment of the surgeon defines the moment for surgery rather than a compelling mandate from uncontrolled bleeding. The second reason for a continuous feeding schedule, and probably of coequal importance with the first, is related to the dividends derived from a very adequate dietary intake. Persons prepared with several days' feeding on a high protein, carbohydrate, caloric, low fat diet, who then must be subjected to an "emergency" procedure, exhibit a greater capacity to withstand both the effects of the bleeding and the operation than do those individuals who, weakened by the bleeding ulcer, are starved as a part of its therapy. Andresen<sup>206</sup> in 1927 was first to propose an active feeding program in bleeding ulcer cases, and he used

rather effectively a gelatin, glucose, cream, milk mixture. The choice of gelatin was unfortunate since it is an incomplete protein, lacking among other amino acids the essential one, tryptophane. To Meulengracht<sup>207-211</sup> belongs credit for arousing a real interest in the issue. At the sixteenth Scandinavian Congress for Internal Medicine in 1933 he reported the first series of cases with hematemesis handled by giving the patient "something to eat." In 1930 and 1935 progressively larger series were reported. In 251 bleeding ulcers there were three deaths (1.2 per cent mortality). His diet consisted of purées, soft foods, and a liberal administration of alkalis. This unorthodox approach to the bleeding ulcer problem intrigued gastroenterologists and was tried at various clinics in America. No group quite attained the remarkable record of Meulengracht but many physicians were able to reduce their local mortality of previous years. The method has not met with universal adoption and debates may linger about certain details, but it is unreasonable to doubt the validity of the major point. It is more scholarly thinking to realize the need for providing a means of neutralizing acid and pepsin, major factors in the genesis and perpetuation of ulcer, than to ignore these items, make no provision for a buffering mechanism, and thereby let nature assume the entire burden of healing, as is done by those who subscribe to the therapy of a starvation regimen. The concomitant advantages secured by providing some nutritious elements are also apparent.

*Cases With Obstruction:* The problem presented by a bleeding ulcer with obstruction, at times, in any one individual case, may seem almost insoluble. It is common experience that in people with such ulcers almost all methods of neutralization are much less effective. Experience in this clinic with the continuous drip has verified this. Because of the obstruction, feeding by this route may avail little or even be impossible, and bleeding in such circumstances has been very difficult to control. A few times, we have employed a saline solution of human thrombin, instilled into the stomach, allowed to remain in place for twenty minutes, and then repeated every six hours. In this very small series, coincidentally, and for the first time, there has been a prolonged abatement in the bleeding, as indicated by serial hemoglobin, hematocrit studies. Conclusions are unwarranted from such circumstances, which may be merely fortuitous, yet the idea seems to merit repetition. All patients with a bleeding ulcer are transfused several times each twenty-four hours until the hemoglobin is brought up to 10 Gm. and then held at or over this figure. Alkalinization of the urine by an intravenous 5 per cent sodium bicarbonate solution *pro re nata*, in order to prevent tubular precipitation of hemoglobin in an acid media, is a part of this transfusion routine. There has been no cause for regretting adoption of this precaution. Charts of the blood pressure and pulse, secured every hour, are kept on all patients with evidence of any real bleeding. Determinations of the hemoglobin and/or hematocrit are secured at least twice daily and more frequently if at all indicated. And, in spite of these precautions and a real interest in the problem on the part of the nursing personnel, medical and surgical staffs, fatal exsanguination has taken place, without detectable, even

in retrospect, premonitory signs, and hence before remedial therapy could avail. The patient past 45 years of age presents a particularly trying problem. In such instances when recent gross weight loss does not complicate the problem, it is probably wisest to control the bleeding through operative measures as soon as transfusions stabilize the pulse rate and blood pressure outside the shock range. Too frequently in this group a stiffened, arteriosclerotic vessel lies patulous in the ulcer bed permitting life to be pumped away with each heartbeat. When there exists, in addition, a real and obvious need for preoperative nutritional measures due to a recent large percentage weight loss, the problem becomes yet more difficult and any "routine" form of management is disadvantageous. One can stoutly affirm that the decision whether and when to operate on certain patients in this category comes closer at times to divine reckoning than to surgical judgment.

Cases 8 and 9, in which the therapeutics were tailored in quite different fashions, are submitted in partial representation of the dissimilarities existing in the bleeding ulcer problem under altered circumstances.

CASE 8 (No. 677891).—T. O., aged 38 years, had had a duodenal ulcer visualized in roentgenograms obtained at the initial visit five years ago before admission. On that occasion he was bothered by recurrent episodes of epigastric distress, and hematemesis had recently been noted. Despite irregular adherence to a reasonable dietary program for the management of ulcer, his gastrointestinal troubles had been minor until recently. Within the few days prior to admission he had had several large tarry stools and repeated emeses said to include 500 c.c. or more of clotted blood. He was bothered by epigastric pain, persistent, moderate, and unrelieved by food. On admission he was noticeably anemic; tarry fecal residue was present in the rectum. The blood pressure was 120/65 mm. Hg and the pulse was 140 per minute. The hemoglobin was 6.9 Gm. per cent and the hematocrit 17 per cent. He was given 500 c.c. of whole blood at once and the following amounts each succeeding twenty-four hours (the hemoglobin changes have been noted in parentheses for each day's transfusions): 900 c.c. (6.95 to 7.3 Gm. per cent); 1,000 c.c. (8.6 to 8.95 Gm. per cent); 1,500 c.c. (9.3 to 12.0 Gm. per cent). In addition, a continuous drip feeding of Diet II via a nasal tube was instituted. After three days this was changed to a drip feeding of an amino acid mixture for two days and finally a sipper arrangement with Diet II when physical and x-ray findings indicated the patient had developed a right, and possibly left, lower lobe pneumonia. This was cared for promptly by penicillin therapy, and fortunately the bleeding had come under control and could be kept in abeyance with frequent feedings via the sipper arrangement. A subtotal gastric resection was performed two weeks after admission, and eight days later the patient was able to leave the hospital.

CASE 9 (No. 749789).—I. S., aged 61 years, gave a four-year history of recurrent attacks of epigastric distress which appeared to be due to a duodenal ulcer repeatedly demonstrated on roentgenograms and confirmed by an exploratory operation performed elsewhere. Six hours prior to admission, while in another hospital, he had vomited an estimated two quarts of blood clots and blood stained material. Shortly thereafter his blood pressure fell to 70 mm. Hg systolic and he appeared to be in a state of shock. Transfusions of blood and plasma were provided until the pressure rose over 100 mm. Hg, at which time the patient was transported to this hospital. Upon admission the hemoglobin was 12.8 Gm. per cent, red blood cell count 4.09 million per c.mm., and the hematocrit 40 per cent. Eight hundred cubic centimeters of plasma were infused during the course of an emergency gastric resection and the pressure and pulse were stabilized well out of shock range. The convalescence was, unfortunately, complicated by a slight amount of bronchopneumonia.

This condition responded rapidly to penicillin therapy and the patient was able to leave the hospital on the tenth postoperative day.

### *Cases With Neoplasms of the Colon, Sigmoid, and Rectum*

Patients with neoplasms of the colon, sigmoid, and rectum frequently, too, have lost much weight, are hypoproteinemic, present difficult nutritional problems, and indeed the surgical procedure necessary for cure may be of a large order of magnitude. Unfortunately, if the condition has already progressed to the stage of complete large bowel obstruction, no election for the time of surgery is permissible. A proximal colostomy for relief of the distended bowel and deviation of the fecal stream must be performed as soon as possible. In a large group of cases without complete obstruction, whatever interval necessary can be spent in securing an adequate preparation. Application of this principle has helped to enlarge the scope of one-stage procedures in colon



Fig. 13.—Sipper apparatus.

surgery. Diets I and II have been found applicable for the preparation of such patients with neoplasms of the large bowel. Entirely without foresight or deliberate selection, these diets turned out to possess a low fecal residue. In retrospect this could perhaps have been anticipated since the protein and carbohydrate are in highly absorbable forms and virtually no cellulose is present to contribute to the stool bulk. It is not to be inferred that they are non-residue diets; however, the fecal mass, even after the ingestion of large quantities of Diets I and II, is moderate and invariably can be satisfactorily evacuated with cleansing enemas in the final preoperative preparation of the bowel. The effectiveness of this simple method has made catharsis generally unnecessary.

An intake of 5,000 to 6,000 calories daily is urged, with the patient taking whatever reasonable proportions of the Diets I and II offer the greatest per-

sonal appeal. To facilitate feedings among the more enfeebled patients, a simple bedside arrangement has been developed (see Figs. 13 and 14). A two-hole rubber stopper is fitted with a glass adapter for an air vent and an angled glass sipping straw, introduced well through the other opening. To this is connected a section of intravenous tubing, a spring clamp to prevent leakage, and a glass mouthpiece.

The arrangements are completed by filling a flat-bottomed 500 c.c. flask with the desired diet, inserting the rubber stopper, connecting the tubing, and immersing the bottle in a bowl containing ice chunks. The mouthpiece can be loosely fastened within easy reach on the patient's nightgown, while the length of tubing permits the reservoir to rest on the adjacent bed table. The accessibility of this convenience has evoked spontaneous favorable comment

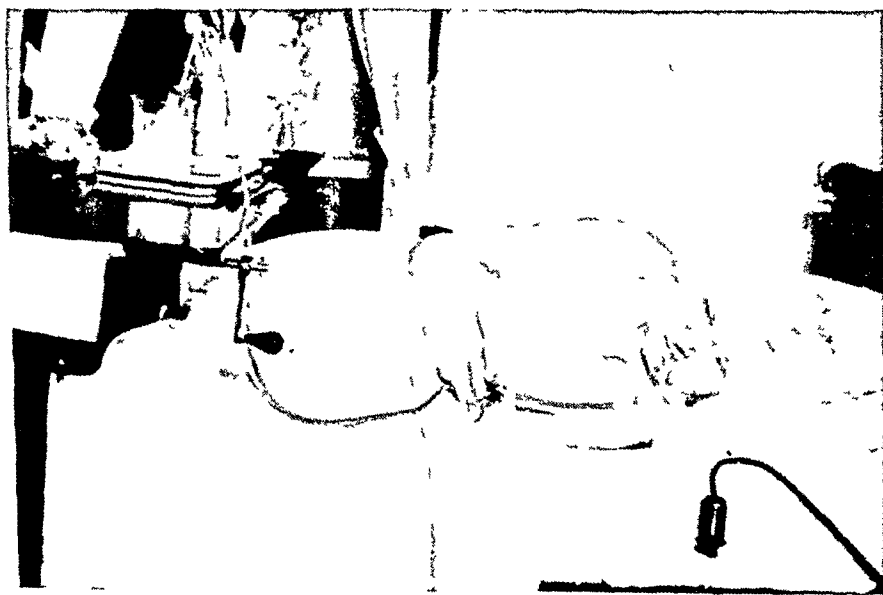


Fig 14.—Sipper apparatus

from patients. The gadget promotes an increased awareness that food is at all times easily available, whereas, otherwise, the simple effort of turning over to reach for food on the bedstand may require too much strength and be abandoned unless a nurse or ward maid is available to carry through the desire. At the same time it avoids some of the disadvantages associated with the prolonged use of an indwelling nasal tube.

#### *Cases of Biliary Tract Disease*

Patients with lesions of the biliary system where hepatic disease is suspected or proved are prepared by feeding a high protein, carbohydrate, caloric, low fat diet. Most instances of common duct stricture or stone, and invariably whenever carcinoma of the duct or head of the pancreas is the preoperative diagnosis, are so treated. There has been no single instance of postoperative



hepatic failure and the convalescence has seemed uniformly associated with less systemic reaction since the institution of this practice. The diet is not always perfectly tolerated by patients with extreme degrees of biliary obstruction. Adding bile salts to the regimen has helped some, but occasionally the diets cause intolerable distress. We have then supplied as much carbohydrate and protein, by the generous use of plasma and amino acids, as possible by the subcutaneous and intravenous routes.

Three case reports pertinent to preparation in such conditions are presented here (Cases 10 to 12).

CASE 10 (No. 739230).—A. B., aged 36 years, had had a cholecystectomy performed elsewhere six months prior to admission. This was followed by a persistent, rather complete, external, biliary fistula, a subphrenic infection, empyema, and a weight loss slightly in excess of 20 per cent of her usual body weight. The subphrenic infection had largely disappeared at the time of admission. The chronic empyema and external biliary fistula were still present. She was prepared for the biliary surgery by supplementing the regular hospital fare with a sufficient quantity of Diet II to bring her daily caloric intake to more than 4,500 calories. This diet averaged about 250 Gm. of protein per day. In addition, bile salts, vitamins K, C, and B<sub>1</sub>, and B complex were provided daily. She gained twenty-five pounds during the several weeks in which this preparation was given and the empyema cured; this cure was effected by establishing complete dependent drainage of the abscess cavity. Postoperatively, after repair of the common duct stricture, some external biliary drainage occurred for a few weeks, but at the time of dismissal this had disappeared, and a cholangiogram indicated that a normal route for bile transit was available.

CASE 11 (No. 726757).—E. J., aged 55 years, had been ill for several years with recurrent bouts of fever and chills. The condition had been treated empirically with sulfonamide compounds, without a diagnosis. During the month prior to admission he had developed anorexia, painless jaundice, a generalized pruritis, and a progressive weight loss. The total weight loss was about 20 per cent of the normal body weight. Nearly every day before admission and during the preoperative hospital stay, he had some fever; this rose on occasion to as high as 104° F. by mouth. On the medical service he received a high protein, high carbohydrate diet of about 2,500 calories daily for about three weeks. He was transferred to the surgical service with the diagnosis favoring a common duct stone. Ten days were devoted to the dietary preparation. Diets IIA and II were used daily to supplement his previous diet so that in excess of 5,000 calories were taken daily. Ample amounts of vitamins B, C, and K and bile salts were added to the oral intake. A Halsted type operation was found necessary when the patient was discovered to have a carcinoma of the ampulla and common bile duct. This included resection of the ampulla, distal portion of the common bile duct, and main pancreatic duct, part of the duodenum, and anastomosis of these ducts back into the duodenal wall. The recovery was without complication. The patient was discharged on the sixteenth postoperative day and has remained well during the ensuing fifteen months.

CASE 12 (No. 733594).—A. W., aged 70 years, five weeks prior to admission developed a painless jaundice, associated with darker than normal urine, light colored stools, a generalized pruritus, and a twenty-pound (about 15 per cent body) weight loss. The clinical diagnosis was carcinoma of the head of the pancreas. The patient was prepared during a period of eleven days for the anticipated biliary surgery by a high protein, carbohydrate, low fat solid diet, plus a liter of Diet II daily. The patient received one transfusion. Vitamins B, C, and K and bile salts were given daily. A single-stage removal of the head of the pancreas, stomach, and duodenum was performed in seven hours and thirty minutes. Throughout the entire procedure the blood pressure was easily maintained at 120 mm. Hg systolic and 60 mm. Hg diastolic, and the pulse rate at 60 per minute, with plasma infused

at a rate equal to the measured blood loss. The postoperative convalescence was hampered and prolonged through an inexcusable technical blunder by myself that resulted in a temporary partial obstruction at the gastrojejunal outlet. At the time of discharge five weeks postoperatively this had cleared up and he was eating a full diet. There was no obvious additional trouble for about six months, but the patient then became cachectic and died.

### *Cases of Hyperthyroidism*

Since the maintenance of normal nutrition in hyperthyroid individuals is hampered by at least two mechanisms (increased rate of utilization and depression of hepatic function) the feeding problem in these cases is doubly important. Weight loss initiated in the past and continuing into the present often, despite therapy with Lugol's solution or thiouracil, bed rest, sedatives, and diets formerly deemed ample, can only be inferred to mean that every day more calories are needed than the individual is ingesting. On the contrary, an uncomplicated gain in weight is a translatable indication that the caloric deficiency has been met. With a growing experience this has come to an ever-increasing significance for us, as a positive sign that such patients, even with severe hyperthyroidism, are ready for any surgery necessary to cure the disease. Stage procedures and polar ligations have found little application in this clinic for more than two years. When the preoperative care has specifically included the use of the high protein, carbohydrate, caloric, low fat Diets I and II, no instance of postoperative thyroid storm has been encountered. Prior to the development of this awareness of the tremendous amount of food that may be required, this complication was encountered. There have been other improvements in the surgical care of hyperthyroid states and therefore it is unfair to suggest that this improvement is related exclusively to modifications in feeding techniques. It does seem pertinent to recount the story of a serious postoperative thyroid crisis, associated with jaundice, hyperthermia, and developing cardiac irregularities, which developed in a patient operated upon without special dietary preparation. During the stormy convalescence, while in an unresponsive condition and with manifest evidence of decreasing hepatic function, he received, among other therapeutic measures, large quantities of Diets II and IIA by nasal tube. Shortly after the institution of this therapy he began to exhibit a gradual progressive recovery with a lowering of the serum bilirubin and general systemic improvement. The dietary feedings were maintained during the remainder of the convalescence which was slow but eventually completely satisfactory. This diet has been tried in another hospital in the management of a severe postoperative thyroid crisis with a similar favorable result.

No further occasions to test the value of this kind of therapy have arisen. Of a certainty, all cases of thyroid crisis do not terminate fatally when no special feeding measures are instituted; yet since the prognosis in this complication is grave, any means possible of benefiting the patient and improving the outcome is worthy of recognition. These patients with severe hyperthyroidism, particularly the exophthalmic variety, are urged to consume sufficient quantities of the Diets I and II, in addition to the regular fare if they so

desire, that weight loss ceases, and better yet, a weight gain is accomplished. This may require 6,000 to 8,000 or more calories every day.

The instance of postoperative thyroid crisis is reported in more detail in Case 13. Other instances of preparation in patients suffering from thyrotoxicosis follow.

CASE 13 (No. 725695).—A. N., aged 55 years, in the year previous to admission noticed a progressive weakness, dyspnea on exertion, excellent appetite but, despite this, a weight loss of fifteen pounds. There was heat intolerance, increased sweating, a tremor of the hands, and prominence in the eyes. A course of deep x-ray therapy to the gland and lugolization had been employed in an attempt to control the hyperthyroidism. Basal metabolic rate determinations during this period were plus 69 per cent, plus 65 per cent, plus 60 per cent, and plus 65 per cent. The ordinary hospital high caloric diet was used in the dietary preparation of this patient on the medical service. His caloric recorded intake, however, was frequently less than 3,500, occasionally less than 3,000 calories daily. Viewed in retrospect, perhaps too little attention was accorded this detail by the surgical consultant and operator. A unilateral subtotal thyroidectomy was performed after fifteen days preparation with Lugol's solution, sedation, bed rest, and this dietary intake. Postoperatively a severe hyperthyroid reaction rapidly developed. The temperature rose to 105° F., jaundice appeared, and the patient was cyanotic and irrational. Thirty-six hours postoperatively, drip feeding with Diet II was started and, augmented by a nearly continuous venoclysis of 20 per cent glucose, more than 6,000 calories daily were provided. Following this therapy there was a steady decline in the serum bilirubin and a gradual improvement in the patient's general condition along with an abatement of the fever. A successful if not smooth convalescence was ultimately secured. Prior to subtotal resection of the gland on the remaining side at a later date, more attention was given to dietary preparation and the recovery postoperatively was without a complication.

CASE 14 (No. 740966).—M. M., aged 35 years, had had a steady increase in the severity of her symptoms of weakness, irritability, nervousness, heat intolerance, sweating, and appetite during the year prior to admission. Many of the classical physical findings of severe hyperthyroidism due to a diffuse hyperplastic goiter were present. The recent weight loss was twenty-five pounds, representing 18 per cent of the body weight. Repeat basal metabolic rate recordings were plus 59 per cent, plus 73 per cent, and plus 53 per cent. Lugol's solution, sedation, bed rest, and a high vitamin B<sub>1</sub> intake were combined with generous portions of Diets I and II, and hospital fare. This patient averaged close to 8,000 calories daily for nineteen days, without significant (less than 0.5 kilogram) weight gain. Bilateral subtotal thyroidectomy carried out after this preparation was followed by an easy convalescence.

CASE 15 (No. 740635).—M. N., aged 64 years, had been bothered by dyspnea and weakness for three to four years before admission. During this interval her appetite had been unusually good. For the past six months she had had insomnia. A known goiter had been present for many years, but lately there was an increase in size of this gland. During the two months prior to admission she noted nausea, would vomit after meals, and found her weakness increasing. Little depression of appetite occurred, however, until this period. A basal metabolic rate secured at that time was plus 50 per cent and a gastrointestinal series of roentgenograms indicated an infiltrating and polypoid carcinoma of the stomach. While awaiting routine admission she developed a lobar pneumonia. Under chemotherapy with sulfamerazine this responded satisfactorily. On the twenty-second hospital day she was transferred to the surgical service. Total weight loss from these several illnesses was over fifty pounds and represented nearly 40 per cent of the usual body weight. It was difficult to make an unequivocal diagnosis of hyperthyroidism clinically. From the laboratory viewpoint there was sufficient gastric obstruction to exclude a galactose tolerance test and the cholesterol

values were of little significance after so much weight loss. Repeat basal metabolic rate studies were plus 78 per cent and plus 56 per cent. Since hyperthyroidism might exist and because she had a moderately severe degree of tracheal obstruction from the nodular gland, thyroidectomy was elected first. A 4,000 caloric diet intake was achieved by using the sipper and Diet II in conjunction with intravenous 10 per cent glucose, amino acids, and plasma (or blood) daily. After two weeks a radical bilateral subtotal thyroidectomy was performed. Recovery was without untoward event. An additional seventeen days were devoted to dietary preparation employing the sipper and Diet II exclusively to achieve a somewhat higher daily caloric intake. An extensive subtotal gastric resection for carcinoma was then carried out. The convalescence was complicationless and the patient was discharged on the ninth postoperative day. There was little weight gain during this preparatory period, but since discharge and return to the outpatient clinic, she has gained steadily and rapidly.

### *Cases of Burns*

The acute need for protein to avoid and to treat the shock rising from burns has been recognized by many.<sup>212-216</sup> It is less generally appreciated that such individuals very soon are in negative nitrogen balance from many causes. Some nitrogen balance studies made in such cases are obviously quite incomplete since no measured values were secured for the amount of protein lost locally from exudation and sloughing.<sup>217, 218</sup> Also, but much less important, no quantitation was made of the protein present in the stool. The intake is reduced by the reluctance of a sick patient to eat. Dressings or pain also may limit the movements attendant with feeding unless special precautions are set up to avoid this situation. There is also an increased nitrogen loss from fever and from the sequestration of necrotic tissues locally at the burn area, as well as from the weeping of protein-containing fluid from the burn site. Unless prompt, effective measures are instituted, these several sources of protein loss may soon generate a severe hypoproteinemia. Wound healing about the burn site is retarded. Of equivalent importance is the fact that split-thickness skin grafts removed from donor sites fail to heal onto these areas. Finally, the donor sites heal slowly or not at all and show an extreme reluctance to grow another full layer of skin. About two-thirds of the total body sulfur is contained in the skin protein. Adults in nitrogen equilibrium<sup>219</sup> on adequate diets can be induced to store considerable amounts of nitrogen and sulfur by superimposition of the proper protein foods on their basal diets. Loss of this material alone from a broadly burned area places a big burden on the protein-synthesizing mechanisms. Diets rich in the sulfur-containing amino acids (methionine and cystine) are particularly necessary, therefore. Patients coming to our plastic service are often already in the stage where they exhibit the chronic effects of the burning. Such patients have been fed diligently Diets I and II, alone or in addition to the regular hospital fare. The beneficial results have become quite apparent. When skin grafting is attempted before adequate nutrition is effected, the results are poorer and healing of all wounds is less satisfactory than when provision is made for an ample period of feeding with a highly protein, carbohydrate, and caloric type diet. Such a feeding program brings about a temporary delay of the necessary reconstructive procedures, but ultimately shortens the required period of hospitalization for a

higher incidence of primary "take" is noted in the grafts, and the donor sites more rapidly regenerate new epithelial layers.

### *Miscellaneous Conditions*

Diets I and II have been applied to the problem of attaining a positive nitrogen balance in a variety of conditions. Its fluid nature is advantageous in the preoperative feeding of patients with esophageal carcinoma. Weight loss from inanition due to obstruction in the esophagus is often a problem in such patients. If necessary a single dilatation can be carried out, but usually the patients are capable of passing on swallows of these liquid diets. From there on the preparation is the same as in all instances of carcinoma of the stomach. Daily intakes of 5,000 or more calories are not unusual. In two instances of esophageal diverticula with a limited food intake associated because of obstruction from the lesion, a nasal tube was threaded past the lesion and the caloric requirements more than met by dripping Diet II into the stomach. Patients with carcinoma of the lip, mouth, tongue, jaw, and neck who are unable to swallow any food postoperatively are satisfactorily sustained in a similar fashion. There is a group of patients with surgical conditions who exhibit a greater tendency to develop diarrhea when oral feedings are urged too vigorously. Included among these are some instances of gastrojejunocolic fistula and regional enteritis, and most of the patients with ulcerative colitis. By exercising moderation and judgment in the pursuance of oral alimentation along with employing Diet II rather than the others in such patients, plus intravenous feedings of glucose, amino acids, plasma (or blood), it has often been possible, nevertheless, to correct amply enough for surgical purposes this nutritional deficiency. In the majority of instances with such preparation, single-stage procedures have been carried through without added hazard. This encompasses a subtotal resection of the stomach, colon, and small intestine followed by the appropriate anastomosis for the gastrojejunocolic lesion, and multiple intestinal resections (often small and large bowel) for the severer cases of regional enteritis. Even the lifesaving procedure of ileostomy for the acutely ill patient with ulcerative colitis, in our experience, is made safer and evokes fewer systemic reactions after adequate efforts directed at nutritional rehabilitation.

As suggested previously, the protein lost through purulent discharges is usually considerable. Patients with a draining empyema, extensive chronic osteomyelitis, or Meleney type of ulceration, are typical of this situation. Such persons are prone to tolerate poorly any necessary surgery. Since an early effect of hypoproteinemia is a contraction of the blood volume, this would conceivably be reflected in an exaggerated response to even slight amounts of blood loss. Our experience has been, though, that if the operation is deferred during a period of dietary preparation, these individuals do then tolerate a very major type of operation. When convinced, by a brief discussion of the importance of their cooperation and the positive contribution they can make by consuming as much of the diet as possible, the patients usually eat large quantities of protein and carbohydrate daily.

Cases 16 to 20 are introduced as evidence that real plasma protein regeneration can be achieved under adverse biologic circumstances. These admittedly are neither exact nor sufficiently critical experiments, yet I believe the data merit consideration for the present and plead successfully the case for additional more detailed observations in the future.

Information pertinent to the protein intake requirements and some of the results obtained by means of daily feedings of large quantities of protein from two sources to a patient with a Meleney type ulcer of the anterior abdominal wall comprise the subject matter in Case 16.

CASE 16 (No. 740032).—K. P., aged 33 years, had a Meleney ulcer, with the edges subcutaneously dissected, which traversed the abdomen from one iliac crest to the opposite side, engulfed the umbilicus, and extended nearly to the costal margin. The progress of the lesion had been associated with a large weight loss, anorexia, febrile episodes, and general bodily and mental deterioration. She was reluctant even to eat when fed by ward attendants, nor would she cry out for medication when in distress. A continuous twenty-four hour a day intragastric drip feeding program with 100 Gm. of powdered bovine plasma\* protein in 500 c.c. of water (Diet IV) and sufficient quantities of Diet II to approximate 4,000 calories daily were given. After one week, these quantities were increased to 200 Gm. of powdered bovine plasma protein and enough diet to provide more than 4,800 calories daily. The hemoglobin value, percentage of plasma proteins, and albumin fraction were secured at the beginning of the feeding, during the course of the project, and at its conclusion. Blood volumes were obtained at the start and finish. These data have been recorded in Fig. 15. The most striking rise in the plasma protein value occurred in the albumin fraction which increased from 2.7 Gm. per cent on June 19, 1944, to 3.7 Gm. per cent on July 12, 1944. While the hematocrit rose from 32.5 per cent on June 19, 1944, to 35.5 per cent on July 19, 1944, the blood volume was enlarged from 3.93 to 5.5 liters during the same interval. It is obvious that plasma protein regeneration was effective by this feeding schedule. The magnitude of the quantities regenerated is hardly appreciated until the factor of increased blood volume is brought into the calculations.† It is then apparent that the total albumin content of the plasma volume was nearly doubled during the test period.

Such data serve to emphasize both the hazard of submitting such a patient with a reduced blood volume to any additional bloodletting and the wisdom of providing for restoration of vascularly retained fluids before surgery is undertaken. Interesting, also, is the seeming failure of the body to act effectively on available protein, that is, there is a progressive rise in the intake-conversion ratio. For instance, increasing the protein content of the diet from the average of 295 to 402 Gm. daily actually contributed but 20 Gm. additional daily to the protein retained by the body since the remaining 85 Gm. were lost through an increased daily excretion of urinary nitrogen. In the presence of a real need for protein fabrication the mechanisms controlling this phase of metabolism find limitation in their own processes of conversion, rather than in the digestive and absorptive abilities of the intestine. This impression is corroborated by very low values obtained in analysis of the stool content for protein nitrogen.

\*Use of this material is an adaptation to clinical therapy of the data of Madden and Whipple (see Table I).

†See legend, Fig. 15.

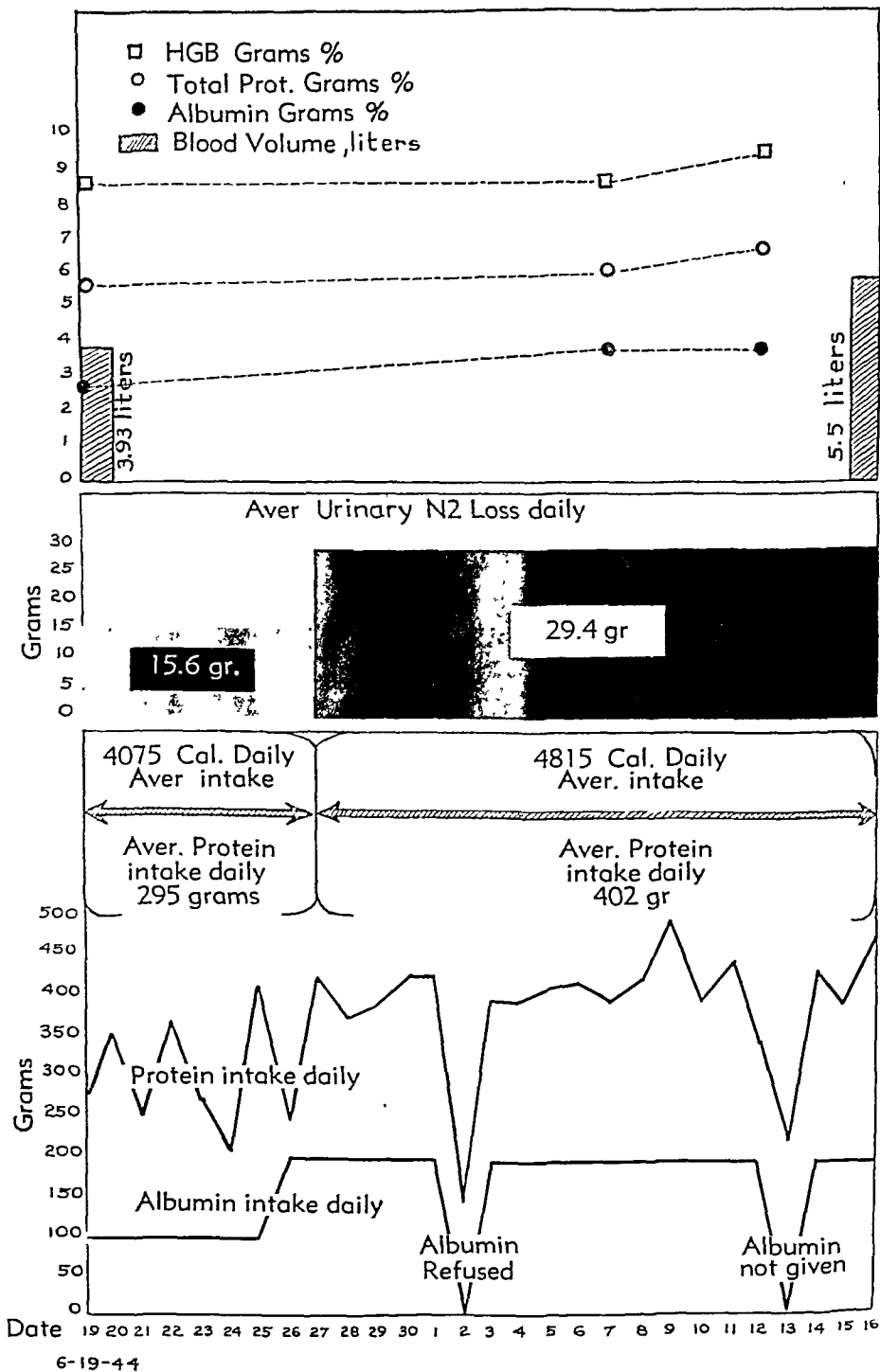


Fig. 15. (Case 16).—Record of total protein intake and plasma protein response. Calculation of albumin gain: blood volume (June 19, 1944), 3.93 liters; hematocrit (June 19, 1944), 32.5 per cent; Plasma albumin fraction (June 19, 1944), 2.7 Gm. per cent; calculated circulating plasma albumin, 71.62 Gm.; blood volume (July 19, 1944), 5.5 liters; hematocrit (July 19, 1944), 35.5 per cent; plasma albumin fraction (July 12, 1944), 3.7 Gm. per cent; calculated circulating plasma albumin, 131.26 Gm.; calculated gain in circulating albumin, 59.64 Gm.

CASE 17 (No. 734359).—F. R., aged 75 years, stated that an indefinite distress in the upper abdomen present for many years had grown during the past two months into an acute, nearly continuous pain, associated with anorexia but no vomiting. Thirty-five per cent of the body weight had been lost recently. X-ray examination of the stomach suggested that a local infiltrating carcinoma of the antrum with retention was present. This degree of obstruction proved to be of no magnitude during the preoperative preparation.

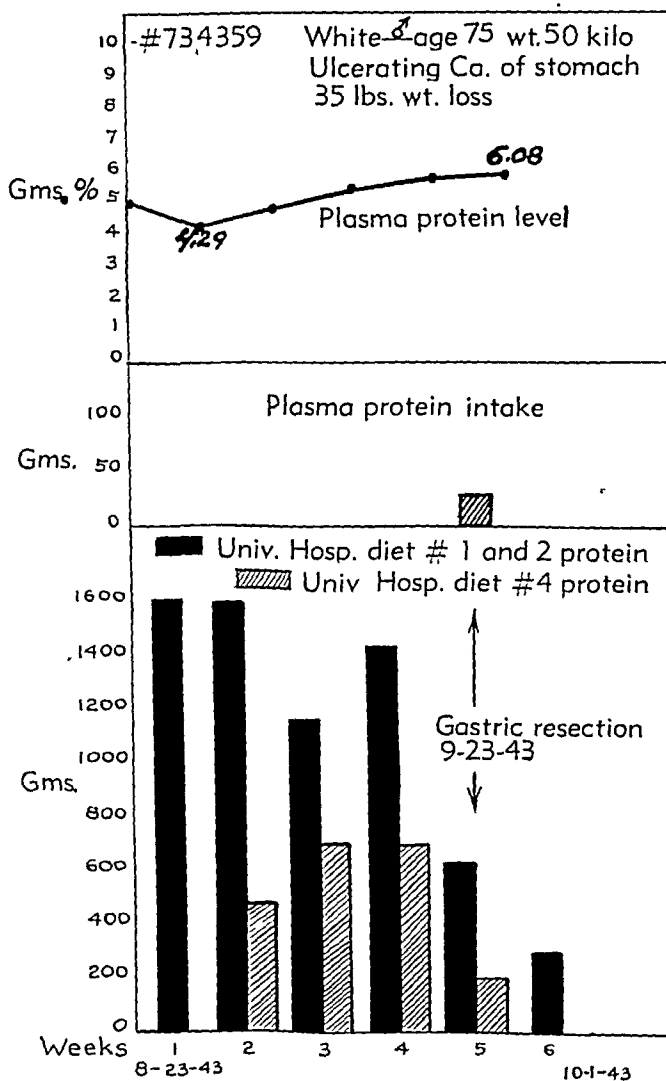


Fig. 16 (Case 17).—Record of total protein intake and plasma protein response.

During the first eight days of dietary therapy nearly 6,000 calories daily were taken in Diets I and II. During this period the plasma proteins dropped from 5.0 Gm. per cent, secured just after beginning the therapy, to 4.3 Gm. per cent one week later. One hundred grams of crystalline bovine albumin in Diet IV were added daily and the caloric intake maintained in excess of 4,000 calories daily with adequate amounts of Diet I. Values for plasma protein secured at approximately weekly intervals during the following twenty-one days were 4.29, 4.9, 5.4, 5.8 (just prior to surgery). (This is about the maximum response



ever secured in these studies from protein feedings with the gastric or duodenal lesion still in situ, to contribute to the regular protein loss.) After this preparation the patient was operated upon, a subtotal gastric resection performed, and a recovery without complications realized. The patient was discharged on the eighth postoperative day.

While studying nutritional problems in surgical patients, the opportunity was realized of treating the hypoproteinemia of a patient with lipid nephrosis.

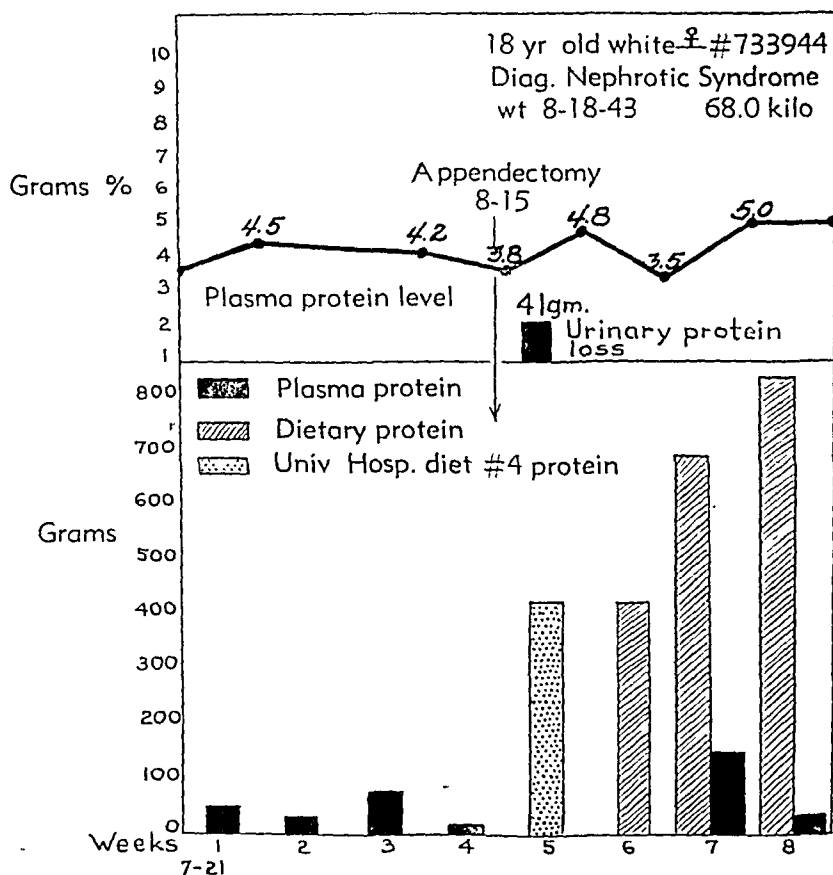


Fig. 17 (Case 18).—Record of total intake and plasma protein response.

CASE 18 (No. 733944).—J. S., aged 21 years, was admitted to the medical service, where a diagnosis of lipid nephrosis was confirmed by clinical and laboratory methods. She developed right lower quadrant pain, tenderness to palpation, and muscle spasm in this region. Appendicitis could not be excluded positively and she was, therefore, operated upon for this condition. During the convalescence she ingested 450 Gm. of powdered bovine plasma protein in Diet IV during a five-day interval, in addition to a diet calorically ample. At the start of the therapy the plasma proteins were 3.8 Gm. per cent. Within twenty-four hours after completing this test period they had risen to 4.8 Gm. per cent. As can be noted in Fig. 17 this gain was achieved despite a urinary loss of about 40 Gm. of protein, determined according to the Esbach technique. At the conclusion of this period she was transferred back to the medical service, where she was placed on salt-free hospital fare with a subsequent steady fall of the plasma proteins to 3.5 Gm. per cent. In excess of 2,250 c.c. of plasma intravenously were then required to restore the plasma

proteins to about the same value they had attained after the feeding of powdered bovine plasma protein.

The apparent increase in the plasma protein value after feeding 450 Gm. of powdered bovine plasma protein might have been achieved through either an increase in the protein intake of the individual or an improvement in the quality of the protein as suggested in the studies of Madden and Whipple. Additional consideration should perhaps have been given to the question of whether the augmented protein intake and subsequent elevation of the plasma proteins were associated with an increased daily loss of protein in the urine. Since the ingestion of the powdered bovine plasma protein was attended by an increase in the plasma protein value, any pyramiding of the urinary loss remained yet small enough to permit a net gain of the plasma protein value. The problem of treating the hypoproteinemia of lipoid nephrosis appears, therefore, intimately related to the quantity of protein ingested and to its innate ability to induce plasma protein regeneration.

Hypoproteinemia, in the absence of ascites, developing in an individual with a Laennec type of cirrhosis, is usually ascribed to an impairment of protein fabrication. While preparing nutritionally just such a patient for the removal of a carcinoma of the colon, observations were made which suggested that under special circumstances even such a pathologically involved liver is capable of elevating a reduced plasma protein value, perhaps even to normalcy.

CASE 19 (No. 723512).—C. G., aged 59 years, was known to have a Laennec type of cirrhosis for at least ten years prior to admission. He had had bouts of jaundice, ascites requiring repeated paracenteses, hypoproteinemia, urobilinuria, and dye retention.

The diagnosis of carcinoma in the sigmoid colon was made before this admission. At that time medical consultants, after securing a number of laboratory tests, noted a depression of hepatic function, probably related to the cirrhosis. For ten days he received on the average of 5,000 calories daily from Diets I and II without raising the percentage of the plasma proteins above the initial level of 5.7 Gm. per cent. During the next nine days the filtered residue obtained from one pound of homogenized raw pork liver was added to the diet, that is, the patient received Diet IIA. This was followed by an increase in the plasma proteins to 6.3 Gm. per cent, an increase associated with augmentation of the albumin fraction as can be noted in Fig. 15. During this second phase of the preparation the caloric intake was maintained high also. After this preparation, exteriorization and excision of the sigmoid lesion was carried out. At the time of exploration the liver was found to be nodular and no larger than the operator's two fists, although the patient's weight was 95 kilograms. Convalescence was smooth from this and from the subsequent closure of the colostomy at a later date. While at home he discontinued the dietary supplement and a fall in the plasma protein value was noted. During this latter hospitalization the patient was again fed the diet containing homogenized raw pork liver, with an apparent elevation of the plasma protein value from 5.25 to 6.3 Gm. per cent. The patient was urged to maintain this special dietary feeding schedule but demurred, finding the diet too unappetizing; about one year after the last surgical procedure he returned on the medical service with an exacerbation of the cirrhosis. Peritoneoscopy at this time indicated a small, coarsely granular, cirrhotic liver.

The data of Madden and Whipple suggest that raw pork liver when fed is capable of evoking a substantial plasma protein regeneration. Under the

special circumstances of a patient with hepatic cirrhosis at least three mechanisms might be involved in accounting for the augmented plasma protein values after feeding the homogenized raw pork liver.

The elevated plasma protein values might be due to: (1) an increased amount of protein in the diet; (2) the introduction of a protein (present in the raw pork liver) which is more efficiently converted to human plasma protein; (3) the ingestion of specific substances in the liver (for example, components of the vitamin B complex) which facilitate plasma protein regeneration either directly or indirectly through improvement of the existing hepatic disease.

The number of patients fed raw pork liver has remained small because the potential danger of causing brucellosis, though remote, is real and therefore can hardly be sanctioned. Pasteurization has not been tried, but would appear to be the best solution to the problem.

CASE 20 (No. 728019).—C. S., aged 53 years, two and one-half months prior to admission, noted a fluctuant area which had developed in the right groin. This had been incised by the local physician but continued to drain and then developed ulceration about the site. The ulcer increased steadily in size, encompassing the entire lower one-half of the abdomen at the time of admission. Bacteriologic studies confirmed the diagnosis of a Meleney type ulceration. She received blood, plasma, and protein in Diet II and protein in the hospital fare. From Fig. 19 it is noted that when this combination of sources was maintained high, there was a simultaneous increase in the plasma protein values. The trauma associated with some necessary surgery for controlling the disease was associated with a fall in plasma protein values. Unfortunately and undoubtedly playing a major contributing role was the contemporaneous reduction in dietary protein since less attention was apparently paid to intake of protein than when the patient was being prepared for the earlier surgery. The values then rose as the diet intake was increased, only to decrease to seriously low levels under a regimen of reduced intake and additional surgery. With the ulcer completely skin grafted by this last procedure, thus removing this source of protein loss, and with an increase again in the total protein intake, there occurred the final elevation of the plasma protein value.

#### *Application of Dietary Preoperative Preparation to Outpatients*

Lately the Diet II has been adapted to the nutritional preparation of the patients while at home awaiting hospitalization. Milk powder is secured by prescription from the drug room. The following instructions are then provided. One-half pound of sugar is dissolved in one quart of skim milk, six eggs are beaten into this, and then eight tablespoons of milk powder are completely mixed into the liquid. Vanilla, cocoa, or chocolate syrup, and one teaspoon of salt may be added to bring about a more desirable flavor if wished. The individual is urged to keep this in a clean (preferably boiled) receptacle, under refrigeration. The resulting total amount yielding in excess of 2,000 calories is to be drunk each twenty-four hours, in addition to any other food taken in the diet. It is felt that with such a provision for an adjustment back to an adequate diet, the deterioration of the patient's nutritional status does not continue during the invariable delay between diagnosis and the time a hospital bed is available.

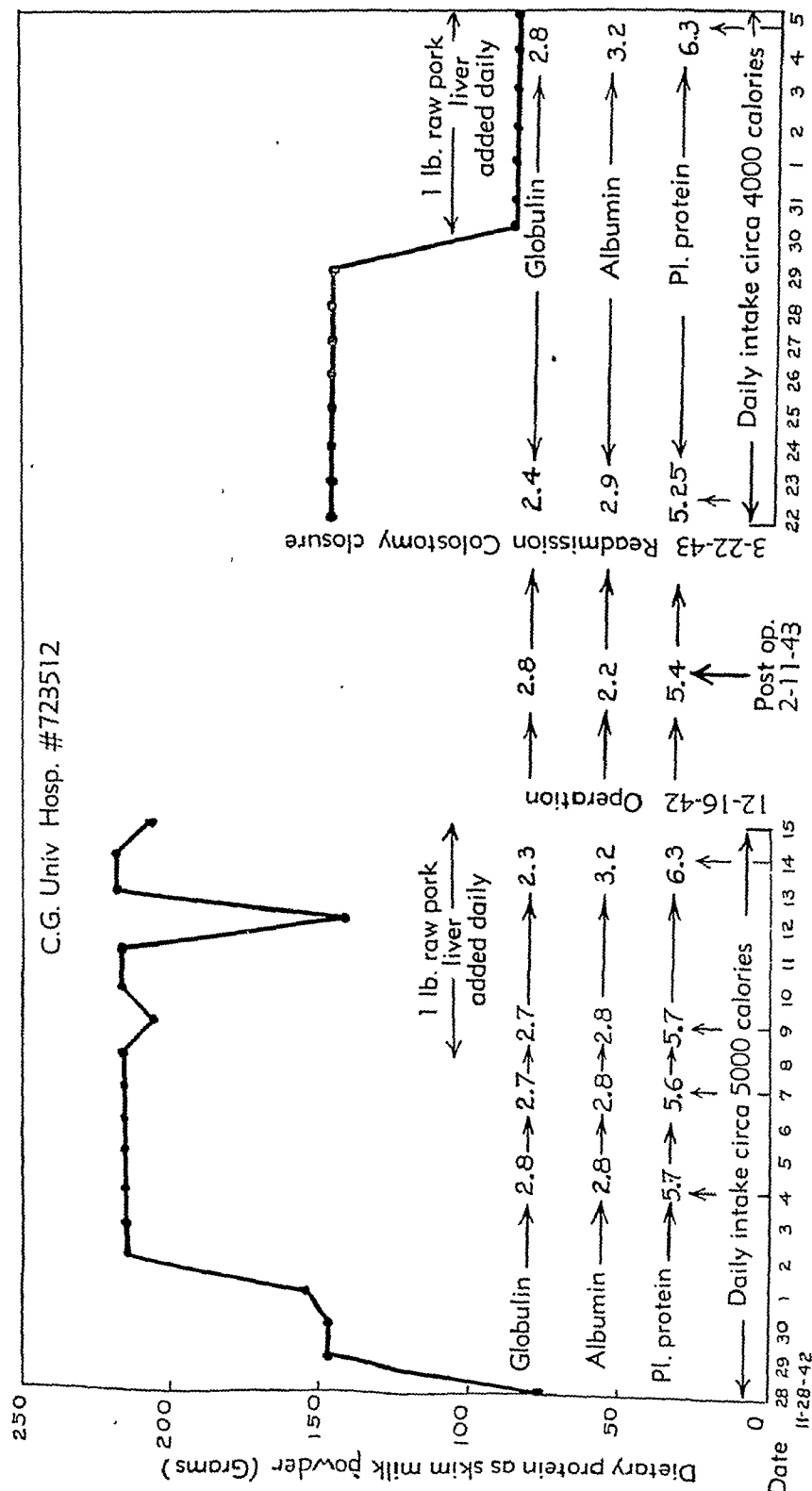


Fig. 18 (Case 19).—Record of total protein intake and plasma protein response.

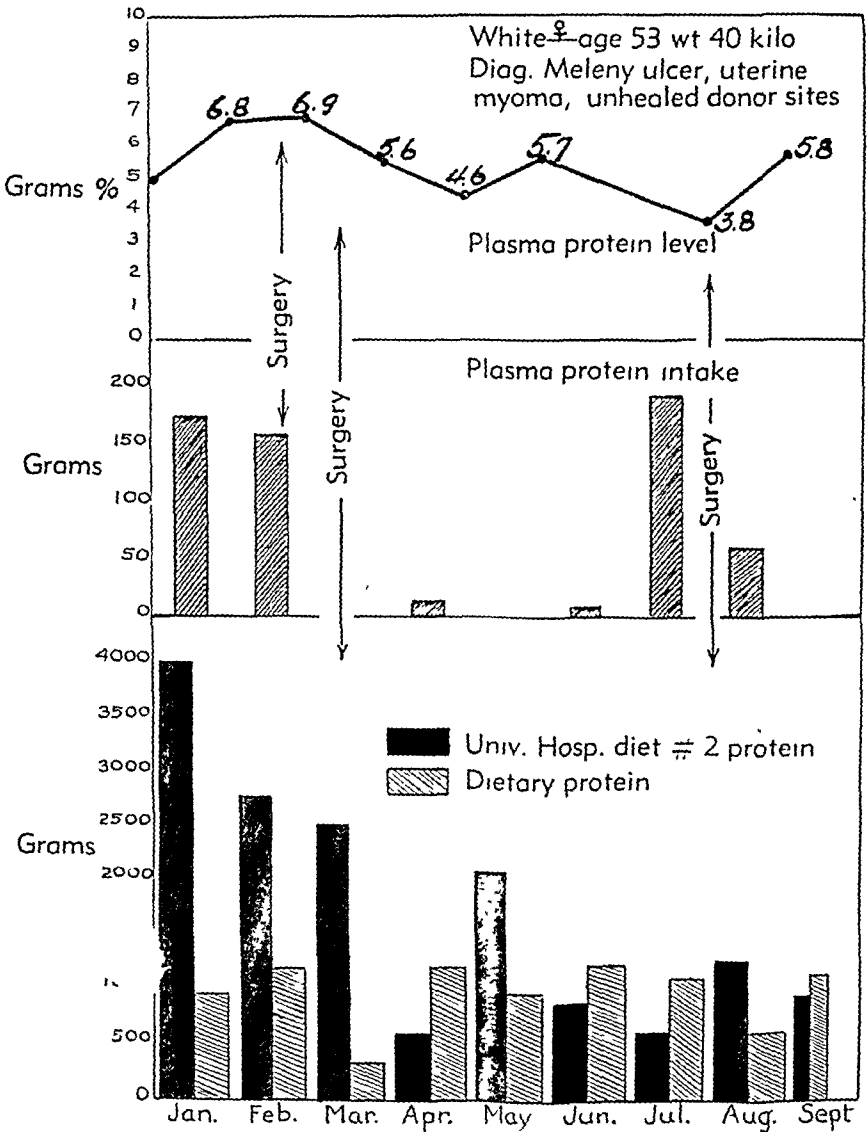


Fig. 19 (Case 20).—Record of total protein intake and plasma protein response.

#### CRITERIA FOR JUDGING DURATION OF FEEDING PROGRAM

Unfortunately, no method of precision is at present available to guide the surgeon in deciding on the length of time preoperatively each patient should be prepared nutritionally. It can, however, be readily appreciated from the foregoing discussion that the loss of body weight is of paramount importance in this calculation. More specifically, the percentile weight loss is the most important and reliable single determining clue found to date. After a limited trial, it appeared that the correlation between biopsy samples secured with the Silverman needle prior to therapy and again at the time of surgery was not enlightening. More efforts are required though to crystallize

this impression. Larger pieces than can be obtained through this type needle, which would be susceptible of quantitative organic chemical analysis, might possibly yield information more readily interpretable. Without submitting patients to an unnecessary operation, no way, as yet, has been found for securing the required control specimens.

Using the percentage body weight as the best index so far encountered, we have come to rely upon the following temporal estimates.\* It is admitted that these are rather empirically selected. However, a growing experience gained from the application of these time intervals to several hundred clinical cases suggests that they are at least long enough to permit an adequate dietary preparation for the most extensive type of surgery.

1. When the percentage of body loss is at least 5 to 10 per cent, three to five days of proper feeding is sufficient.

2. When the percentage body weight loss approaches 20 per cent, ten to twelve days of proper feeding are necessary.

3. When the percentage body weight loss approximates 25 to 30 per cent, nearly three weeks of adequate feeding are required.

4. When the percentage weight loss is in excess of 35 per cent, at least one month of thorough feeding is needed. In this classification is included patients too weak to sit, stand, talk, or feed themselves. When prepared according to this schedule, they are customarily discharged from the hospital after about the same length of postoperative sojourn as those without such a handicap to overcome.

#### SUMMARY

In summary it may be stated that the application to clinical material of the wealth of carefully acquired and accurately documented biologic information on the pathologic physiology of starvation states has been woefully neglected. The therapeutic problems initiated by starvation states are broad and touch on many aspects of the surgeon's sphere of activity. A failure to recognize and appreciate the importance of the concomitant effects that may develop from an inadequate nutrition (fatty liver, decreased hepatic function, hypoproteinemia) materially pyramids the hazards of surgery in that individual. On the contrary, an adequate preparation with appropriate diets lessens significantly these dangers. Without such preparation, the surgeon either must refuse these individuals even surgical procedures of necessity, because of the appreciated added hazards from such an undertaking, or, when persuaded to operate during a default in judgment, he is often led into tragic consequences. On the contrary, we have come to believe that these "poor-risk" cases can be conscientiously accepted for operative procedures of almost any magnitude tolerable to standard-risk cases without augmenting seriously the risk accepted by them—if good dietary preparation has been achieved. From much animal experimentation, it was inferred that a diet rich in proteins, carbohydrates,

\*In individuals with complete pyloric obstruction, being fed exclusively by the parenteral route, it is often wisest to compress the preparation into a fourteen- to sixteen-day period.

and calories, but low in fat would be most likely to afford the greatest protection and provide the best nutrients for restoration to normalcy of the involved structures. Diets have been proposed which embody these considerations. The high protein content has been achieved by fortifying several vehicles with milk powder, which contains all the essential amino acids. Similarly, lactose, cane, beet sugar, are cerelese was added to attain the high carbohydrate content. The fat content has been reduced to minimal values. The two diets developed on this plan most frequently employed are Diets I and II. Diet I is palatable and comes in multiple servings during the day. Diet II is designed to function for tube feedings, is less palatable, but is taken readily by mouth by almost all patients. These diets have been used in the routine care of several hundred patients hospitalized upon both a general and a gastroenterologic surgical service. Large quantities, by volume and caloric content, of such formulas were found to be well tolerated. They have appeared to exert very beneficial effects in correcting some of the pathologic changes secondary to an inadequate, poorly selected caloric intake. Preparation with such diets has been the added factor which permits the surgeon greater license in the magnitude of the operative procedure he may undertake for a cure, and greater freedom to extend the indications for palliative surgery, all without accepting a discouraging increase in mortality. With vigilant attention to such details as hemostasis, blood and plasma replacement commensurate with manifest losses, and careful maintenance of the proper depths of anesthesia, the surgeon can complete his task in a leisurely, meticulous fashion free of the obligation to operate "with an eye on the clock."

These details have also functioned to improve the ravages of bodily structure caused by a wide variety of disease conditions per se (burns, empyemas, Meleney ulcers). Suggestions have been offered to guide the preoperative dietary management of surgical patients with diseases of the gastrointestinal tract.

Particular emphasis was placed on the therapy for lesions of the stomach and duodenum. The special problems related to pyloric obstruction and bleeding associated with lesions in this region received detailed comment and tested therapeutic hints were appended. Feeding of Diets I and II was noted to be a satisfactory form of preparing nutritionally the majority of patients with surgical conditions encountered in the intestinal tract. The bowel residue after such feedings was found to offer no problem during required colonic surgery. This method of preparing patients was applied to those with disease of the biliary tract (stone, stricture, or carcinoma), in instances of hyperthyroidism, and several other surgical conditions. The impression was expressed that recovery from the surgery was more certain and the convalescence more swift than when such dietary preparation was neglected.

The percentage body weight loss is believed to be the best single consideration in determining the duration of the feeding program. Estimates, relative to this percentage weight loss, of the length of time the feeding period should be continued are suggested. Precise functional tests or crucial experimental

proofs of these considerations, however, have not been, as yet, attainable. Man, even under ideal conditions, is a difficult biologic organism to standardize. The problem is additionally complicated by the several hiatuses that exist in our knowledge of protein metabolism generally and specifically in human beings. Since, also, several of those mechanisms originally producing the functional derangements of metabolism (fatty liver, hepatic dysfunction, hypoproteinemia) continue to influence unfavorably normal processes during periods when, through diet, the re-establishment of normal metabolism is sought, the ultimate result will be the balance attained by destructive and constructive forces. Our present efforts suggest, but with no more concrete proof than that of clinical results, that major efforts directed at nutritional readjustment can be made to yield a margin of safety for the patient requiring surgery, in spite of previous, and with coexisting deleterious influences on, metabolic processes. It is apparent that such measurements should be secured; in particular, the rate of development and reversal of pathologic cellular changes in the liver, information concerning the factors governing these changes, knowledge of the intimate regulating mechanisms accelerating and depressing protein anabolism.

Despite the lack of confirmatory evidence obtained under rigid experimental conditions indicating that dietary preparation lessens the risks of formidable operations, the clinical evidence on this score is overwhelming as suggested in a number of the case reports detailed in this study. It has been pointed out that patients who have lost considerable weight are not good candidates for operations of magnitude after adjustment of water, electrolyte, and hemoglobin values. On the contrary, if, in addition, the nutritional deficit of the patient is repaired, such patients tolerate prolonged operation well. Adequate dietary preparation of poor-risk patients who have lost considerable weight does away with the element of hurry in operations. These lessons learned in the school of experience when adopted as standard practice in the preparation of surgical patients will have a telling favorable influence in extending the benisons of surgery to borderline groups of surgical risks without increasing materially the surgical mortality. The surgeon must school himself in the intricacies of dietary preparation of patients as well as in evaluating water and electrolyte balance and in mastering surgical technique.

#### CONCLUSIONS

1. Many patients with gastrointestinal lesions remediable by some surgical procedure present nutritional problems.
2. When a large amount of body weight has been lost by such an individual, the hazards of surgery are increased.
3. Surgery in these patients can be performed at approximately the same mortality as in the standard-risk patient when adequate dietary preparation has been achieved.
4. An adequate dietary preparation can be achieved in these patients, especially when no obstructive element is present, by the utilization of high protein, carbohydrate, caloric, low fat diets.



5. Diets described in the text fulfill these criteria and perform satisfactorily this preparation.

6. Special dietary problems are posed by the patients with obstruction at the gastroduodenal outlet.

7. A satisfactory nutritional preparation can usually be achieved in these patients by employing methods outlined in this study.

8. Special problems of feeding and hemostasis are involved in those patients with bleeding ulcers of the stomach and duodenum. These problems are related to the severity of the hemorrhage, the age of the patient, and presence or absence of obstruction. Suggestions are offered relative to the care of such patients.

9. The need for, and applicability of, such diets in the nutritional preparation of a variety of surgical states is discussed.

10. Broad, empirical rules (but so far the best indices we have) based on the percentage of total weight lost are proposed.

11. The need for securing incontrovertible proof, under better controlled experimental conditions than the clinic affords of the observations related herein, attesting the value and importance of adequate dietary preparation of surgical patients, is suggested.

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## ALKALINE PHOSPHATASE AND METASTATIC LIVER DISEASE

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ALKALINE phosphatase as a diagnostic aid in metastatic carcinoma in the liver has been recorded in the past few years.<sup>1, 2</sup> While serving as a resident on the surgical service of the Presbyterian Hospital of Chicago, I had the opportunity of studying another series of cases, which is the subject of this communication. This test has been employed on all patients with carcinoma on whom it was anticipated there would be an exploratory operation in order that our clinical findings might be checked with the laboratory.

Alkaline phosphatase has been found in greatest amount in osteogenic tissue, renal epithelium, and epithelium of the small intestine,<sup>3</sup> thus, tissues involved in bone formation or in glucose absorption or elimination. It is not found in normal liver cells or bile ducts.

It is possible to produce a carcinoma of the liver in rats by feeding them dimethylaminoazobenzene.<sup>3, 4</sup> In their normal liver endothelium phosphatase is present in small quantity while there was a large amount of the phosphatase found histologically in the endothelium between the newly formed carcinomatous duct tissue. Even the cytoplasm of the carcinoma cells in the liver contained it. This latter may, however, be a specific reaction peculiar to the species since the same tumors reproduced in mice failed to show the high phosphatase content.<sup>5</sup>

In human beings,<sup>3</sup> very little phosphatase was shown in a carcinoma of the breast, whereas it was found in abundance in an adenofibroma and in normal lactating breast tissue. Furthermore, the only phosphatase in a sigmoid carcinoma was found in the surrounding vascular endothelium while in the metastases it was marked in the surrounding endothelial tissue. The hypothesis of these authors concerning the presence of the phosphatase about vascular endothelium was that this tissue contributed to or removed it from the blood stream.

Since it is known there are many forms of liver disease which will give rise to a high alkaline phosphatase, theories have been proposed to account for this. One concept is that the retention of enzymes is due to anything which blocks the excretion of the particular organ. Thus it would be expected that biliary obstruction due to a common duct stone would produce a high phosphatase. This occurs. Other theories maintain that the increase is due to altered liver function. Whether tumor nodules would actually block phosphatase excretion is not known and as yet it cannot be stated just how the phosphatase rises with biliary obstruction.

With this work in mind we have followed eighty-five consecutive cases of carcinoma taking an alkaline serum phosphatase level in each case in an

TABLE I. CARCINOMA WITH LIVER METASTASES AND HIGH ALKALINE PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PER CENT		DISEASE	REMARKS
			PHOSPHATASE	PROTHROMBIN		
7	56	M	36.0	--	Carcinoma of rectum	Liver filled
17	49	F	34.5	--	Carcinoma of rectum	Liver filled
26	54	F	30.0	100	Carcinoma of sigmoid	Liver filled
35	47	M	22.8	--	Carcinoma of sigmoid	Many nodules
36	54	F	24.9	--	Carcinoma of rectum	Many nodules
37	56	M	21.8	70	Carcinoma of rectum	Liver enlarged at death
57	48	M	30.0	100	Carcinoma of rectum	Liver filled, found at cholecystectomy, carcinoma 3 yr. before
61	55	M	22.5	80	Carcinoma of rectum	Liver filled
62	49	F	49.8	--	Carcinoma of rectum	Liver filled
72	41	F	30.0	80	Carcinoma of breast	Liver filled at autopsy
76	66	M	48.6	75	Carcinoma of sigmoid	Liver now nodular, icteric index 84
77	49	M	21.3	--	Hypernephroma	Liver filled
84	66	M	14.2	--	Carcinoma of rectum	Liver filled
92	57	M	15.7	--	Carcinoma of liver	Liver filled
93	48	F	34.5	80	Carcinomatosis	Liver filled

TABLE II. CARCINOMA WITH NORMAL LIVER AND HIGH PHOSPHATASE, ELEVATED ICTERIC INDEX

CASE NO.	AGE (YR.)	SEX	PER CENT		DISEASE	REMARKS
			PHOSPHATASE	PROTHROMBIN		
34	56	F	14.2	--	Carcinoma of rectum	Postoperative peritonitis, icteric index 24 taken at time of phosphatase
46	48	M	42.0	90	Carcinoma of ampulla of Vater	Liver free, icteric index 132
75	67	M	90.0	70	Carcinoma of duodenum	Liver free, icteric index 15

TABLE III. CARCINOMA WITH LIVER METASTASES AND NORMAL PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PER CENT		DISEASE	REMARKS
			PHOSPHATASE	PROTHROMBIN		
4	63	F	9.3	100	Carcinoma of rectum and ovary	Many liver nodules
11	57	M	9.3, 6.3	60	Carcinoma of rectum	Several nodules
14	67	F	6.7	100	Carcinoma of cecum	Several nodules
27	63	M	8.2	100	Carcinoma of cecum	Few nodules
32	39	F	4.8	--	Carcinoma of breast	3 large nodules and multiple bone metastases
53	53	M	4.1	100	Carcinoma of cecum	Many nodules

TABLE IV. CARCINOMA WITH A QUESTIONABLE NODULE IN THE LIVER AND NORMAL PHOSPHATASE

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
9	52	F	8.2	100	Carcinoma of sigmoid	Single nodule, questionable
22	70	M	2.7	40	Carcinoma of rectum	Single nodule, questionable
50	30	F	3.1	--	Carcinoma of rectum	Single nodule, questionable
82	62	F	7.7	100	Carcinoma of ascending colon	Single nodule, questionable

attempt to predict liver involvement. We have twenty-six cases in which carcinoma was not the problem but where the patient was hospitalized for other disease and used as a control or had known liver disease other than metastases. These 111 cases have all been proved by exploration or, in a few cases, by autopsy.

TABLE V. PHOSPHATASE READINGS IN PATIENTS WITH LIVER DISEASE OTHER THAN CARCINOMA

CASE NO.	AGE (YR.)	SEX	PHOSPHATASE	PROTHROMBIN	DISEASE	REMARKS
1	55	F	70.5	90	Common duct obstruction	Long-standing jaundice icteric index 20
2	56	M	25.8	100	Catarrhal jaundice	Icteric index 171
3	58	M	45.7	100	Hypertrophic cirrhosis	Icteric index 19
8	57	F	22.8	--	Common duct stone	Icteric index 12
16	54	M	26.2	--	Cholecystitis	Icteric index 18

Of the 85 cases, wherever we found the alkaline phosphatase elevated (King Armstrong units, 13 being the upper limit of normal) and ruled out certain other diseases such as cirrhosis, obstructive jaundice, or bone disease, there was metastatic disease in the liver. There were fifteen cases which fell into this category although one of these patients had jaundice with the metastases whereas the others did not.

TABLE VI.\* PATIENTS WITH CARCINOMA

Number of patients	57
Liver	Normal
Phosphatase	Normal

\*Individual cases not charted.

In our series there were six cases in which there was definite, and at times marked, liver involvement with a normal phosphatase. We are unable to explain these findings. There were additionally four patients with a questionable single, small liver nodule and a normal phosphatase.

TABLE VII. NORMAL PATIENTS

Number of patients	21
Liver	Normal
Phosphatase	Normal

An attempt to correlate prothrombin determination with liver involvement gave no findings of significance.

In conclusion, as a routine test when dealing with a known malignancy and in the absence of jaundice, known liver disease or abnormal osteogenic activity, a high phosphatase will probably help in establishing the operability of a surgical case. Perhaps a more important use will be in checking post-operative patients to determine late liver involvement without subjecting them to exploration.

#### SUMMARY

1. Alkaline phosphatase in a series of eighty-five cases of carcinoma is presented.

2. Where there was a high phosphatase—and other forms of liver disease such as obstructive jaundice, cirrhosis, and bony involvement could be ruled out—the test showed metastases in all of our cases.

3. Normal phosphatase, however, does not rule out liver metastases.

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# PULSATING HEMATOMA, FALSE ANEURYSM, AND ARTERIOVENOUS FISTULA DUE TO WAR INJURIES

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THIS presentation is not meant to be an exhaustive treatise on the subject of vascular injuries and their sequelae in battle casualties. Rather, it is an analysis of experience with vascular injuries on the surgical service of this general hospital in the Southwest Pacific Theater of War to which casualties were admitted from the campaigns for the Philippine Islands. Four thousand and forty surgical battle casualties (wounded in action) were admitted to this general hospital over a five-month period of time from Oct. 25, 1944, until March 25, 1945. Included with these were twenty patients with severe injury to the peripheral vascular channels of the torso or extremities resulting in false aneurysm, pulsating hematoma, or arteriovenous fistula. The incidence of traumatic vascular lesions of the peripheral circulation in this series of cases is .49 per cent. The types of vascular lesion are listed in Table I.

The diagnosis in these cases, the surgical management, the presence of complications such as nerve injury, contracture of joints, or secondary hemorrhage, and the indications for surgical intervention presented a variety of problems, the solutions of which were intensely interesting as well as challenging. Bearing in mind the dictum that, in the management of vascular injuries, operation should be postponed until collateral circulation has been established so that major vessels may be ligated and divided safely, attention was directed primarily toward the healing of wounds and the establishment of collateral circulation. However, it was necessary to operate upon fifteen of these patients at this general hospital. Early operation was performed only in those patients in whom external or internal hemorrhage endangered life or the viability of an extremity, in those in whom contracture developed rapidly, or in those in whom there was progressive paralysis of peripheral nerves intimately in association with the vascular lesions.

In these twenty patients in whom arteriovenous fistula, false aneurysm, or pulsating hematoma developed as a result of war wounds, the majority of the injuries were caused by small caliber bullets or small shell fragments. Eleven of the vascular tears were caused by Japanese artillery shell fragments, five by Japanese .25 caliber rifle bullets, one by a .30 caliber rifle bullet, two by .31 caliber Japanese machine gun bullets, and one by a .50 caliber machine gun bullet.

## ARTERIOVENOUS FISTULA

There were ten arteriovenous fistulas. Seven of these were caused by Japanese artillery shell fragments, two by Japanese .25 caliber rifle bullets, one

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TABLE I. TYPES OF VASCULAR LESIONS

LOCATIONS	NUMBER OF CASES
Arteriovenous aneurysm	8
Arteriovenous aneurysm and secondary pulsating hematoma	2
False aneurysm	4
False aneurysm and secondary pulsating hematoma	2
Pulsating hematoma	4
Total	20

by a .30 caliber bullet. Hemorrhage from the wound at the time of injury was severe in three patients, mild in six, and insignificant in one. The diagnosis was established by the detection of a to-and-fro murmur at the site of swelling prior to admission to this hospital in only five of the patients. In three the diagnosis was established for the first time on the day of admission to this hospital and in two the bruit was not heard until two weeks after admission and approximately four weeks after injury. In these cases the area of the swelling was examined with a stethoscope but no bruit could be heard in the early weeks following injury. As the days passed, a to-and-fro murmur became audible and increasingly intense, coincident with the development of venous dilatation. It is thought that these were cases of pulsating hematoma which subsequently developed into arteriovenous fistula. In three cases a metallic foreign body had been removed from the extremity prior to the admission of the patient to this hospital. Débridement had been done in the forward areas on only one of these wounds.

Listed in Table II are the locations of the arteriovenous fistulas or aneurysms between concomitant arteries and veins.

TABLE II. LOCATIONS OF ARTERIOVENOUS FISTULAS OR ANEURYSMS

LOCATIONS	NUMBER OF CASES
External iliac artery and vein	1
Femoral artery and vein, middle third	3
Femoral artery and vein, upper third	1
Posterior tibial artery and vein, middle third	2
Posterior tibial artery and vein, lower third	1
Internal carotid artery and jugular vein	1
Brachial artery and vein, lower third	1
Total	10

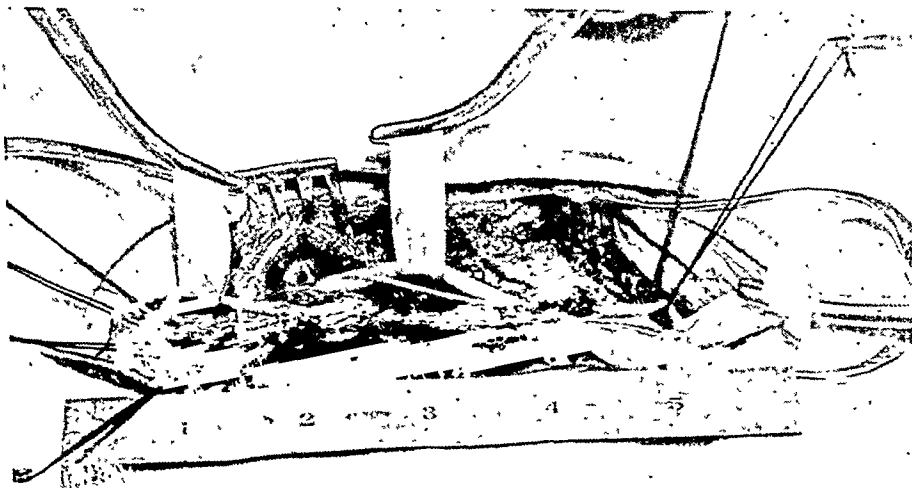
#### CASE REPORTS

##### *Arteriovenous Aneurysm of the Posterior Tibial Vessels*

CASE 1.—A 27-year-old infantryman was struck in the left leg by a .25 caliber Japanese rifle bullet on Oct. 20, 1944. The missile entered the posterolateral aspect of the calf in its middle third and lodged subcutaneously on the medial aspect of the calf at the same level. Surgical débridement was not done but the wound was dressed with sulfanilamide powder. On November 6 the bullet was removed under local anesthesia. Scar of the operative incision is shown in Fig. 1, A. Troublesome hemorrhage from the wound was controlled by suture of the incision. Twenty-four hours after this operation, sedation by morphine was necessary because of pain about the operative site. On examination at this hospital on November 27, there was a palpable thrill over the elevated tissue about the scar on the medial aspect of the



A.



B.

Fig. 1 (Case 1).—A, Photograph showing the scar of the left leg which represents the site from which a bullet was removed before the diagnosis of arteriovenous fistula was made. The operative note stated that there was "profuse bleeding" at the time of the removal of the foreign body. Although the fistula was a large one which afforded communication between the posterior tibial artery and several concomitant veins, there is no superficial venous dilatation. B, Photograph taken at the time of operation shows an arteriovenous aneurysm between the posterior tibial artery and several adjacent veins. The umbilical tape on the right supports the proximal posterior tibial artery. That in the middle retracts the posterior tibial nerve and the tape on the left identifies the posterior tibial artery distal to the aneurysm. The silk ligatures identify three veins proximally and four veins distally, all of which communicated with the aneurysm.



calf. A to-and-fro bruit could be heard over this area. The dorsalis pedis and posterior tibial pulses were palpable. There was no difference in the blood pressure in the two lower extremities. Oxygen saturations of specimens of venous blood from the right and left femoral veins were 60 and 70 volumes per cent, respectively. Teleroentgenograms of the heart taken at a six foot distance showed no cardiac enlargement and no change in cardiac diameters when the fistula was compressed. The pulse rate dropped from 80 to 74 beats per minute when the fistula was compressed. Blood pressure before manual occlusion of the arteriovenous fistula was 120/64 and after occlusion it was 130/70. There was hyperesthesia over the dorsum of the left foot. Progressive increase in the degree of swelling was noted. In preparation for operation the popliteal artery was compressed against the head of the tibia for fifteen minutes four times a day. On January 9 the lesion was excised at operation. Fig. 1, B is a photograph taken at the operating table. The arteriovenous fistula represented a communication between the posterior tibial artery and several adjacent veins. The opening in the artery was at a point just distal to the branching off of the posterior peroneal artery. The fistula had enlarged to an aneurysm measuring one inch in vertical and one half inch in transverse diameters. Three veins communicated with the aneurysm on its proximal end, and distally there were four communicating veins. The posterior tibial nerve was adherent to the aneurysm but its continuity was intact and there was no neuroma. The aneurysm was excised after secure ligation of the afferent and efferent arteries and veins. It was interesting to note that measurements of the diameters of the artery and the largest vein were as follows: proximal artery  $\frac{1}{4}$  inch, proximal vein  $\frac{1}{4}$  inch, distal artery  $\frac{1}{4}$  inch, distal vein  $\frac{1}{4}$  inch. After excision of the lesion the distal stump of the posterior tibial artery pulsed forcibly. The circulation in the foot was so good following operation that block of the lumbar sympathetic ganglia was not deemed necessary. The patient made an uneventful recovery and was transferred to the United States for further convalescence two weeks after operation.

In this case the bruit undoubtedly was present from the time of injury and the operative removal of the bullet probably was the cause of secondary enlargement of the arteriovenous fistula.

*Arteriovenous Aneurysm of the Posterior Tibial Vessels With Subsequent Rupture and the Development of Secondary Pulsating Hematoma*

CASE 2.—An infantryman was struck in the middle third of the left leg by an artillery shell fragment on Jan. 3, 1945. Hemorrhage from the wound was slight. First-aid treatment was given but débridement was not done. The diagnosis of arteriovenous fistula of the posterior tibial vessels was made at a field hospital on the seventeenth day after injury. The patient was admitted to this hospital one month after injury. There was a to and fro bruit over the posterior aspect of the left leg in its middle one-third. The pulses were normal in the foot. There was no disturbance of function of the peripheral nerves. The pulse rate decreased from 116 to 96 beats per minute on compression of the fistula. Teleroentgenograms taken at a six foot distance showed no abnormality of cardiac diameters either before or after manual occlusion of the fistula. Oxygen saturation of the femoral venous blood was 64 volumes per cent on the affected side and 46 on the normal side. On the thirty-fourth day after injury the patient complained of pain in the calf for the first time. There was obvious increase in swelling of the calf. The dorsalis pedis and posterior tibial pulses were still palpable. At operation on February 16 the specimen shown in Fig. 2 was removed. The sudden attack of pain in the calf was explained by a secondary rupture of the arteriovenous fistula. The constricting musculature of the soleus and gastrocnemius muscles accounted for the curious hourglass contour of this arteriovenous aneurysm and pulsating hematoma. The older aneurysm lay between the muscular layers of the tibialis posterior and the soleus while the communicating hematoma was encapsulated between the soleus and the gastrocnemius muscles. The lumbar sympathetic ganglia were blocked with novocain before the patient

left the operating room. Circulation of the affected extremity was ideal but the patient developed moderate contracture of the Achilles tendon and embarked for further convalescence in the United States two months after operation.

This case record calls attention to the possibility of secondary rupture of traumatic arteriovenous aneurysms. The patient was confined to bed at the time of the onset of the pain which was coincident with the secondary internal hemorrhage.

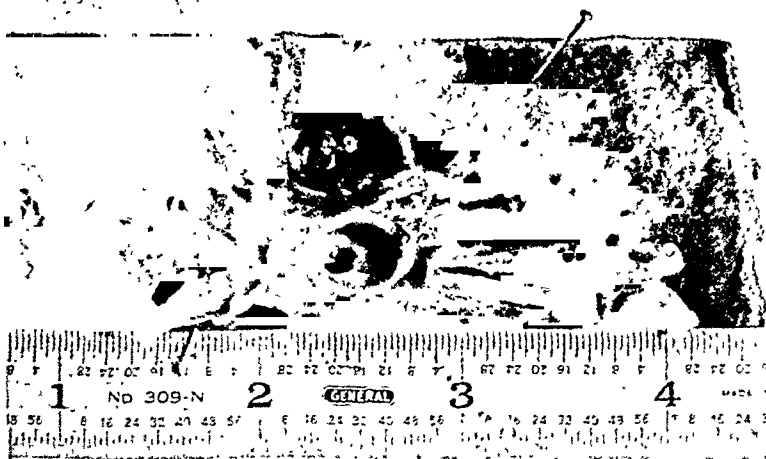


Fig. 2 (Case 3) showing the specimen removed from patient. This is an arteriovenous aneurysm of the posterior tibial artery and several adjacent veins. The pins identify the aneurysmal sac and communicating veins. The aneurysmal sac has an hourglass shape due to the formation of the original aneurysm which is immediately in communication with the vessels and the upper more recent aneurysm which developed at the time of secondary hemorrhage thirty-four days after the injury. The upper sac contained clotted blood. In the center of the lower sac, the openings into both arterial and venous channels can be seen.

#### *Arteriovenous Fistula of the Posterior Tibial Vessels With Subsequent Rupture and the Development of Secondary Pulsating Hematoma*

CASE 3.—A soldier was injured Jan. 25, 1945, by a Japanese .25 caliber bullet which entered the posterolateral aspect of the middle one-third of the left calf and made its exit on the lateral aspect of the medial one-third of the calf. There was severe hemorrhage at the time of the injury. There were no fractures or nerve injuries. He complained of pain from that time on and was admitted to this hospital on Feb. 11, 1945, with the classical signs and symptoms of arteriovenous fistula at the middle one-third of the left calf on its medial aspect. The diagnosis of the vascular lesion was established at the time of admission to this hospital. The extremity is shown in Fig. 3, A. There was a moderately distant to-and-fro murmur, of which the patient was conscious. The radial pulse was 85 per minute. After compression of the aneurysm it was 76. Oxygen saturation of the venous blood from the affected leg was 62 volumes per cent, and 51 from the normal side. He was kept in bed in this hospital and the popliteal artery was compressed for fifteen minutes four times each day. On March 5, while awaiting evacuation, the patient had sudden sharp pain in his calf and that area became more swollen. The dorsalis pedis and posterior tibial pulses no longer could be palpated. With the diagnosis of internal bleeding from the arteriovenous aneurysm the calf was explored on March 6. A vertical incision was made over the medial aspect of the calf posterior to the tibia. There was a large pulsating swelling 4 by 6 cm. in size, occupying a space between the soleus muscle and the tibialis posticus group. The posterior tibial

nerve was intimately adherent with this mass. The mass was almost exactly in the mid-portion of the calf. In an attempt to dissect around the aneurysm and to define the efferent and afferent arteries and veins, the thin-walled aneurysmal sac was broken into. Thick clot and fresh blood gushed forth. Tourniquet was applied and the dissection was continued. It was found that there was some shredding of the fibers of the margin of the posterior tibial nerve but that its continuity was intact. The proximal artery measured only 2 mm. in diameter and the proximal vein was 3 mm. in diameter. The distal artery and vein were of similar size. The communicating opening in the artery was 1 cm. long. The aneurysmal sac was composed of two portions, a small sac measuring 2 by 1 cm. which apparently had been formed by the limitations of the tibialis posticus muscle and a

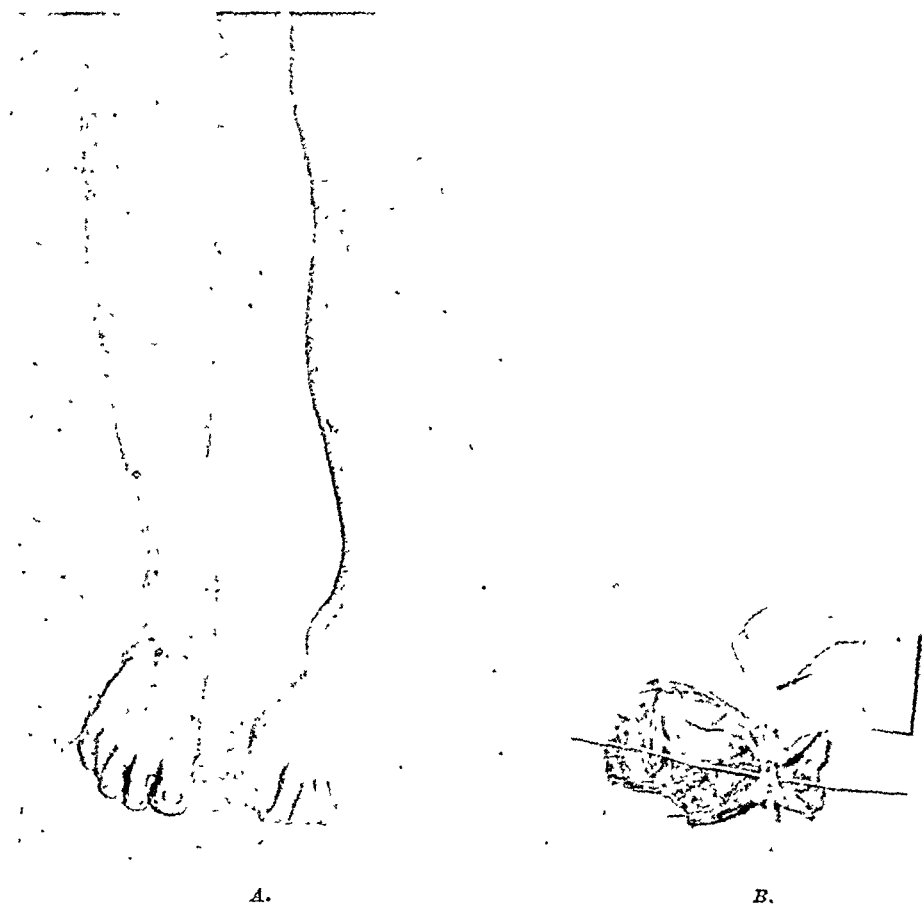


Fig. 3 (Case 3).—A, Photograph showing the degree of swelling of the left calf due to arteriovenous fistula between the posterior tibial artery and vein. Injury was caused by a Japanese .25 caliber bullet which entered the posterolateral aspect of the left calf in its middle one-third. The scar represents the point of exit. The fistula had formed a false aneurysm 2 cm. in diameter between the tibialis posticus and the soleus muscles. Although the patient had been kept in bed, the arteriovenous aneurysm had ruptured thirty-nine days after the original injury. Extending from the ruptured arteriovenous aneurysm three was a pulsating hematoma approximately 4 by 6 cm. in size lying in the fascial plane between the soleus and gastrocnemius muscles. The apparent foot drop is due to contracture of the tendo Achilles. There was no associated nerve injury.

B, Photograph of specimen of arteriovenous aneurysm of the posterior tibial artery and vein. The wires are inserted into the artery (right tag) and vein (left tag) which are transversely placed. The vertical probe demonstrates the arteriovenous communication. The aneurysm has an hourglass shape due to the fact that the lower, smaller sac which contained circulating blood had ruptured on the thirty-ninth day after injury to give rise to the upper thin-walled sac which was filled with clotted blood. The lower sac was limited in its development by the confines of the tibialis posticus muscle fibers while the upper, larger sac lay in the plane between the gastrocnemius and the soleus muscles.

larger more recent sac 5 by 4 cm. in size between the soleus and gastrocnemius muscles. The specimen is shown in Fig. 3, B. This larger sac was filled with clotted blood. Apparently it had developed when the patient experienced pain the day before operation. Quadruple ligation was done with zero black silk. The aneurysm and its adjacent vessels were excised. The abnormal arteriovenous communication was of the posterior tibial artery and vein at a point between the muscular branches and the posterior malleolar branch. The patient convalesced uneventfully except for the development of moderate contracture of the Achilles tendon. He was transferred to the United States for rest and recuperation forty-three days after operation.

The sequence of events and the pathology in this case are almost identical with those in Case 2.

*Arteriovenous Aneurysm of the Brachial Vessels; Partial Paralysis of the Median Nerve*

CASE 4.—A 25-year-old infantryman was struck in the lower third of the left arm by a .25 caliber Japanese rifle bullet on Feb. 24, 1945. Severe hemorrhage from the wound was treated by compression dressing. The patient was conscious of a whirring sensation in his arm just above the elbow at the time of admission to this hospital on March 24. There was a "machinery murmur" and a palpable thrill over the medial aspect of the lower third of the arm. Compression of this area did not alter the resting pulse rate of 80 per minute, the blood pressure (which was 120/80), or the cardiac diameters as demonstrated by teleroentgenograms taken at a distance of six feet. Oxygen saturation of venous blood taken from the cephalic vein on the affected side was 85 volumes per cent and on the normal side it was 45. Examination of the hand showed impairment of function of the sensory and motor components of the median nerve. There was slight secondary enlargement of the compressible swelling of the arm on April 14, forty-eight days after injury. At operation, April 16, an arteriovenous aneurysm between the brachial artery and two adjacent veins was excised. The opening in the artery was just distal to the origin of the superior ulnar collateral artery and it was not possible to save that important vascular branch. The aneurysmal dilatation extended for a distance of 3 cm. along the tract of the missile. The median nerve was firmly bound to the aneurysm by fibrous tissue. A small neuroma was excised from this nerve. The aneurysm was removed by quadruple ligation and excision. The ligated distal end of the brachial artery pulsated but the radial pulse was not palpable until twenty-four hours after operation. The circulation in the hand was excellent following operation. Novocain block of sympathetic ganglia was not necessary. Although the condition of the arm and hand were approximately normal, it was necessary to transfer the patient to the United States for convalescence from associated thoracic injury.

*Arteriovenous Fistula Between the External Iliac Artery and Vein*

CASE 5.—A 26-year-old infantryman was injured on Dec. 7, 1944. A .30 caliber enemy rifle bullet struck the Browning automatic rifle which he was carrying. Fragments of the bullet amputated the distal phalanx of his right ring finger and entered the tissues of the right groin. Immediate hemorrhage from the wound was slight but the patient recalls the gradual development during the next few days of a painful swelling in the groin. Within a few hours after injury he was treated at a clearing station where metallic fragments were removed from the wounds and the saphenous vein was ligated. December 24, he was admitted to the hospital, the wounds appearing as shown in Fig. 4, A. Thick-split grafts were applied to the wounds promptly. The appearance after grafting is shown in Fig. 4, B. The loud to-and-fro murmur and the thrill were maximal in intensity just above the inguinal ligament. Oxygen saturation of venous blood was 70 volumes per cent on the affected side and 45 on the normal side. There was no impairment of nutrition of the foot and the peripheral pulses were palpable though weak on the side of the affected leg. Direct compression of the fistula was reflected in a drop in pulse rate from 74 to 62 per minute and a change in blood pressure from

120/56 to 120/70. This maneuver, however, did not effect any change in cardiac diameters as shown by teleroentgenograms made at a distance of six feet. During the period while this patient was awaiting evacuation to the United States, the circulation in the fistula was occluded for ten-minute periods four times daily by direct pressure on the abdominal aorta.

In this case there was no episode of secondary bleeding and therefore no indication for operative intervention while the patient was in this hospital. Interest in this case centers on the fact that, although the fistula was a large one, still there was no sign of development of cardiac dilatation during the three and one-half month period of observation. Also, it was interesting to note that thick-split grafts afforded protection against external hemorrhage.



Fig. 4 (Case 5).—A, Furrowed wound of the groin caused by a .30 caliber bullet. Just above the upper wound, there was a palpable thrill and a loud "machinery" murmur. Because of the danger of severe secondary hemorrhage, the wound was skin grafted promptly. B, Showing the appearance of the wounds after application of thick-split grafts. X marks the point of maximal intensity of the murmur.

#### *Arteriovenous Fistula of the Femoral Vessels, Upper Third*

CASE 6.—A 25-year-old infantryman was injured in the left upper anterior thigh by Japanese 90 mm. mortar shell fragments, Jan. 24, 1945. There was severe hemorrhage from the wound at the time of injury. Within two hours débridement was done at an evacuation hospital. He was admitted to this hospital on Feb. 11, 1945. The wound was healed and there were no symptoms, but swelling in the left femoral triangle was associated with the characteristic signs of arteriovenous fistula. The diagnosis was established for the first time at this hospital. Oxygen saturation tests of the blood were not done but Branham's sign was positive. The pulse rate dropped from 88 to 68 on manual compression of the fistula. Teleroentgenograms showed no cardiac enlargement and no change in cardiac dimensions after compression of the fistula. The peripheral pulses were present in both feet and nutrition of the foot on the affected side was normal. Collateral circulation was encouraged by frequent compression of the femoral artery against the head of the femur proximal to the fistula. There

was no secondary swelling and no other indication for operative intervention at this station. The soldier was transferred to the United States for further care thirty-five days after admission.

*Arteriovenous Fistula of Internal Carotid Artery and Jugular Vein*

CASE 7.—A 23-year-old infantryman was struck by an enemy shell fragment in the right side of the neck on Jan. 30, 1945. The shell fragment entered the neck just anterior to the upper third of the sternocleidomastoid muscle and lodged lateral to the body of the third cervical vertebra. There was significant hemorrhage from the wound. Emergency care was given at a field hospital where the diagnosis of arteriovenous fistula was made one day after injury. The characteristic to-and-fro murmur was heard over the upper portion of the anterior cervical triangle. Compression of the fistula was reflected by a drop in pulse rate from 88 to 84 and a rise in blood pressure from 120/80 to 130/85. Teleroentgenograms taken at a six-foot distance showed no cardiac dilatation and there was no variation in cardiac dimensions after manual obliteration of the fistula. The patient was conscious of a buzzing sensation in the right side of the neck. The optic fundi were normal. There was no venous dilatation. There were no episodes of pain or secondary swelling and no indication presented for early surgical intervention. The patient was transferred to the United States for further care.

*Arteriovenous Fistula of the Femoral Vessels in Their Middle Third*

CASE 8.—A 28-year-old private in a chemical battalion suffered multiple wounds of the right thigh from Japanese artillery shell fragments, Jan. 20, 1945. There was mild hemorrhage from the wounds. Early treatment consisting of sulfanilamide dressings was carried out at a clearing station within one hour after injury. The diagnosis of arteriovenous fistula was made on a hospital ship enroute to this base. On admission to this hospital on February 25, examination showed that the wounds were healed. The bruit and murmur characteristic of arteriovenous fistula were present over Hunter's canal in the middle third of the thigh. There was no significant dilatation of the veins of the affected leg. Branham's sign was positive; the pulse rate dropped from 96 to 80 on compression of the fistula. There was no cardiac dilatation as measured by teleroentgenograms taken at a distance of six feet and compression of the fistula did not cause any change in cardiac dimensions. The patient was given regular treatments consisting of compression of the femoral artery against the head of the femur for twenty minutes every four hours until April 18, the date on which he embarked for the United States by hospital ship.

In this case there was no sign of secondary rupture of the fistula and no indication for early surgical intervention.

*Arteriovenous Fistula of the Femoral Vessels, Middle Third*

CASE 9.—A 25-year-old sergeant, attached to a tank battalion, was wounded in the right thigh by fragments of a Japanese hand grenade on Feb. 7, 1945. There was severe hemorrhage from the wound of entrance over the anterior aspect, middle third of the right thigh. He was treated at an evacuation hospital and transferred to this base via hospital ship. The diagnosis of arteriovenous fistula was made for the first time on admission to this hospital, February 27. The patient was conscious of a buzzing in the thigh and complained of constant mild pain in the thigh. Evidence of nerve damage existed in that there was loss of dorsiflexion of the great toe. Branham's sign was positive, the pulse rate dropping from 92 to 80 after compression of the fistula. Regular vascular exercises to promote collateral circulation were given as in Cases 7 and 8, and the patient embarked via hospital ship for the United States on April 18.

*Arteriovenous Fistula of the Femoral Vessels, Middle Third; Division of the Saphenous Nerve*

CASE 10.—A corporal in the Philippine Army was wounded by artillery shell fire on Oct. 23, 1944. Information regarding treatment prior to admission to this hospital was incomplete,

the records revealing only that the wounds were dressed and sulfadiazine was administered. On November 2, physical examination showed that the wound of entrance was on the medial aspect, middle one-third of the right thigh, and that the wound of exit was on the lateral aspect of the thigh at the same level. There was flexion contracture of the knee as shown in Fig. 5. Within a few days the wounds were healed. There was a palpable thrill and a loud to-and-fro murmur over the medial aspect of the middle third of the thigh. Compression of the femoral artery against the head of the femur caused the bruit to disappear. Compression of the

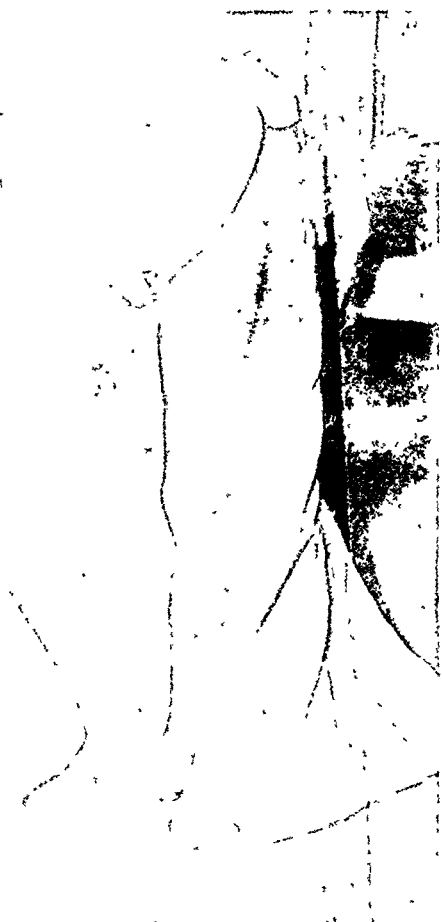


Fig. 5 (Case 10).—Photograph showing the degree of flexion deformity of the knee caused by arteriovenous fistula of the femoral artery and vein in their middle thirds. The patient is holding the right knee in full active extension.

fistula itself was followed by a drop in pulse rate from 96 to 80 per minute and by a rise in blood pressure from 102/60 to 112/62. However, teleroentgenograms taken at a distance of six feet after compression of the fistula showed no difference in the measurements of the cardiac shadows. There was no cardiac dilatation. The veins of the lower leg were distended. The popliteal, dorsalis pedis, and posterior tibial pulses were palpable. For thirteen weeks prior to operation, the patient was treated by frequent compression of the femoral artery against the head of the femur in order to promote the development of collateral circulation. The patient was necessarily held in this hospital pending orders from the Philippine Army for his transfer. At operation, January 31, the fistula was found to have developed between the femoral artery and vein at a point just proximal to the highest genicular artery. The fistula had undergone aneurysmal dilatation. It measured 2.7 cm. in transverse diameter.

There were a number of collateral veins which communicated with it. The continuity of the saphenous nerve had been interrupted by the missile and the frayed ends of the nerve were adherent to the fibrous sac of the aneurysm. Quadruple ligation and excision of the aneurysm were done. Incision of the specimen showed that in it there were several loose clots. The saphenous nerve was sutured. Novocain block of the lumbar ganglia on the affected side was done. The circulation in the foot was satisfactory after operation but on the fifth post-operative day the patient died from a massive pulmonary embolus. Post-mortem examination showed that there was a thrombus in the femoral vein proximal to the point at which it had been ligated.

In only two of these cases was there associated impairment of peripheral nerve function. One of these was the <sup>1</sup> the brachial vessels which showed partial loss of motor and sensory function. <sup>2</sup> median and ulnar nerves. In another case there was complete division of the <sup>3</sup> venous nerve in association with an arteriovenous fistula of the femoral vessels. This is of interest in view of the fact that nerve injuries were more frequent in the patients with false aneurysms in this series. Studies on the effects of the peripheral fistula on the vascular system showed that Branham's sign was positive in nine of the ten patients. In all of the ten there was persistent tachycardia ranging from a pulse rate of 80 per minute to 110 per minute. In the patients with femoral arteriovenous fistula the average drop in pulse rate following compression of the fistula was 16 beats per minute. In those with posterior tibial arteriovenous fistula the corresponding average was 12. In the one patient with external iliac arteriovenous fistula the drop in pulse rate on compression of the fistula was 12 per minute. Compression of the fistula of the brachial vessels was not reflected in relative bradycardia. These observations do not contribute any evidence to support the teaching that the size of the fistula and its proximity to the heart are in relationship to the degree of tachycardia present and to the degree of bradycardia which follows compression of the fistula. Moreover, at the time of admission to this hospital (an average of twenty-one days after injuries were sustained) none of these patients showed cardiac enlargement or variation of cardiac diameters as measured by teleroentgenograms taken at a distance of six feet before and after compression of the fistulas. It is clear from this evidence that the cardiac dilatation which is referred to often as an invariable secondary effect of arteriovenous fistula is not present soon after the development of these vascular abnormalities. The impression obtains that this complication develops slowly and progressively secondary to persistently increased volume flow of blood through the heart. Pain in the involved extremity was a symptom in four cases. Flexion deformity of a neighboring joint was a significant finding in only one of these ten cases. This observation is of interest in view of the fact that of the ten patients with false aneurysms, five developed flexion contractures soon after injury. The characteristic "machinery murmur" or "to-and-fro bruit" was present on auscultation over the involved area in all ten cases of abnormal arteriovenous communication. In only four cases was the patient conscious of a thrill over the involved area. In three of these patients there was an episode of increasing pain over the involved area with secondary increase in regional swelling. The underlying pathology in these cases proved to



be an hourglass type of aneurysm due to secondary rupture of the aneurysmal arteriovenous communication, the newly formed hematoma being limited in its development by the fascial sheaths of another anatomic plane. In five of the ten patients in whom specimens of venous blood were taken from the involved extremity and from its fellow there was increased oxygen saturation on the involved side. In all patients attention was directed toward the development of collateral circulation by frequent compression of the artery proximal to the fistula. In three cases it was necessary to operate because of the complication of secondary swelling. In a fourth case a small fistula was excised by quadruple ligation of the lower posterior tibial vessels and the patient was returned to duty. The fifth patient, who was operated upon, was a Philippine soldier who spent three months at this station awaiting transportation to a hospital in the Philippine Islands. During this period collateral circulation was established by regular periods of compression of the artery proximal to the fistula. The fistula then was excised. There were no peripheral vascular complications following surgical excision of the fistulas in these five patients. In two of them, however, contracture of the Achilles tendon developed following excision of fistula of the posterior tibial vessels in their lower one-third. Of these ten patients with arteriovenous fistula, five were transferred to the United States for operative treatment and five were operated upon in this general hospital without peripheral circulatory complications but with one death due to pulmonary embolus. The average elapse of time between dates of injury and operation was sixty-one days. One of these soldiers was returned to duty and two others might have been returned to duty except for the presence of associated injuries which required a prolonged period of convalescence.

#### FALSE ANEURYSM AND PULSATING HEMATOMA

Since false aneurysm and pulsating hematoma are complications secondary to incomplete lacerations of arteries, these cases have been grouped together in this presentation. There were ten cases in all. In three there were well-developed false aneurysms which had ruptured secondarily with resultant formation of a secondary pulsating hematoma. Four were examples of false aneurysms with well-developed fibrous sacs containing circulating blood. In three patients with pulsating hematoma, the clot had plugged effectively the tangential tear of the artery and had not yet undergone liquefaction.

The surgical management of these patients presented a variety of problems. While awaiting the development of collateral circulation the indication for operation presented when sudden pain and increased swelling about the vascular lesion indicated that a secondary hemorrhage into the tissues had taken place. This occurred in five of the ten cases. In three of these the swelling was of such degree that pulses peripheral to the lesions were no longer palpable. In these cases operation was performed as an emergency procedure. In a sixth case, brisk hemorrhage from a granulating wound overlying a false aneurysm necessitated exploration. Progressive dysfunction of involved peripheral nerves constituted the indication for operation in three additional patients. In the tenth case a

small aneurysm of the brachial artery was discovered during operation as neurolysis of the median nerve was being done.

Five of these incomplete arterial lacerations were caused by small artillery shell fragments. Two were caused by .25 caliber Japanese rifle bullets, two by .31 caliber Japanese machine gun bullets, and one by a .50 caliber machine gun bullet. In all cases the missiles were small. Immediate hemorrhage from the wound was mild in nine patients and severe in one. The diagnosis was made prior to admission to this hospital in only one case. This is explained easily since it has been our observation that the systolic bruit characteristic of pulsating hematoma and false aneurysm may not be present in the early days following injury. It has been observed that the true pulsating hematomas, those in which the clot has not liquefied, give rise to a bruit which is only faintly audible. As the false aneurysmal sac forms and the clot liquefies, the bruit becomes more intense. In all of these cases of false aneurysm and pulsating hematoma, pressure on the bell of the stethoscope caused the bruit to disappear and the distal pulses to be no longer palpable. The average number of days which elapsed between injury and diagnosis was seventeen.

Five of these vascular lesions were of the brachial artery, one was in the second portion of the axillary artery, one was of the radial artery, one was of the posterior tibial artery, one was of a muscular branch of the femoral artery, and the tenth aneurysm arose from the ulnar artery.

#### CASE REPORTS

##### *False Aneurysm of the Radial Artery With Impairment of Function of the Median Nerve*

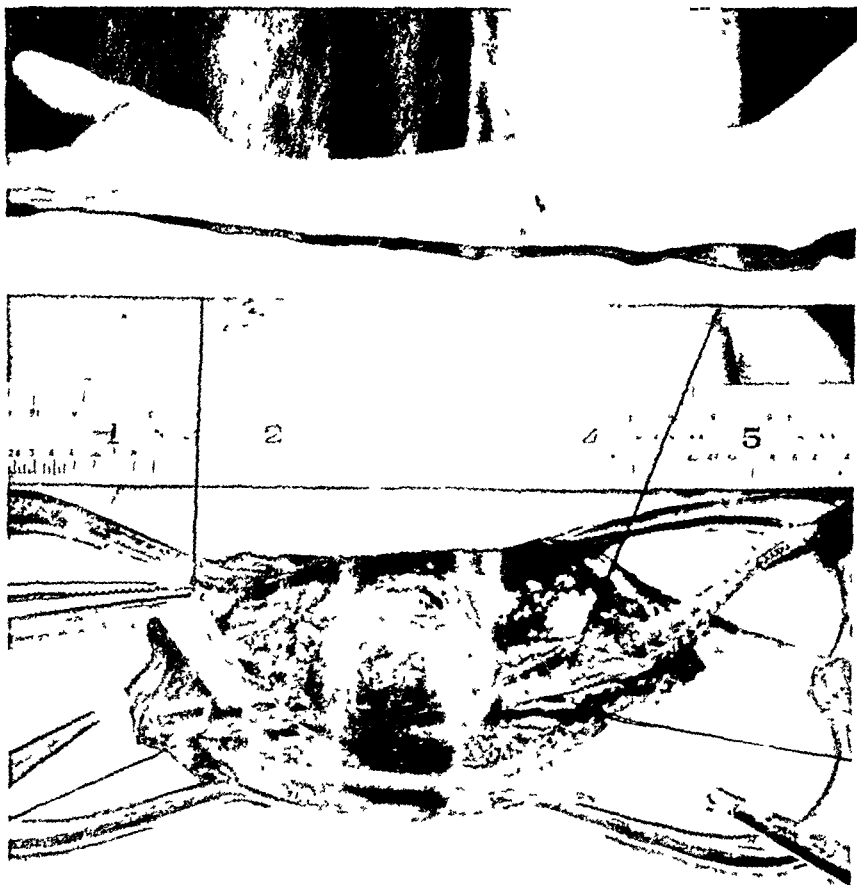
CASE 11.—A 19-year-old infantryman sustained a penetrating wound of the left forearm from an enemy hand grenade fragment on Dec. 17, 1944. Débridement was done at a clearing station and the soldier was admitted to this hospital Jan. 7, 1945, at which time the diagnosis of false aneurysm was made. Painful swelling had been noted since the second day after injury. There was an expansile, pulsating swelling 4 cm. in diameter over the radial side of the middle third of the flexor surface of the right forearm. The arm is shown in Fig. 6, A. There was a systolic bruit over this swelling and pressure on it caused obliteration of the radial pulse. There was hyperesthesia over the area of the hand supplied by the median nerve and movements of the fingers were coarse. For this reason the lesion was exposed at operation on Jan. 24. The median nerve was embedded in fibrous tissue around the false aneurysm which was 2.5 cm. in diameter. A photograph was taken at the operating table (Fig. 6, B). It was noted that the artery measured only 2 mm. in diameter proximal to the aneurysm but was 3.5 mm. in diameter distal to the aneurysm. Despite the thin fibrous coat which constituted the aneurysmal sac, it was possible to dissect it out completely and to excise it with a segment of artery. The concomitant vein was ligated and divided. Examination of the specimen showed that the rent in the artery was 3 mm. in diameter. The sac contained a central clot and free blood peripherally. There were no striae lining the false aneurysmal sac as is seen in similar lesions which have been present for a longer time. Following excision of the lesion, the radial pulse was palpable at the wrist. The soldier was given intensive physical therapy to the hand and was returned to duty at his own request on May 1, with full function of the hand.

##### *False Aneurysm of the Brachial Artery With Compression of the Median Nerve*

CASE 12.—A 34-year-old infantryman was struck in the left arm on Oct. 25, 1944, by a .25 caliber Japanese rifle bullet which entered the anteromedial surface of the arm and made

its exit from the posteromedial surface. There was an expansile, pulsating swelling over the medial aspect of the middle one third of the left arm and a fairly loud systolic bruit could be heard over this area. Pressure on this swelling caused obliteration of the pulses distally. The patient complained of pain at the site and there was limitation of extension (20 degrees) of the elbow. Blood pressure taken at the right arm was 115/70, while on the left it was 70/40. Because of the progressive anesthesia of the palm, the patient was operated upon December 15. The median nerve was found to be firmly adherent to the fibrous mass which represented the false aneurysm. The nerve was dissected away and was found to be intact. The aneurysm, which was 4 cm. in diameter, arose from the brachial artery just distal to the point at which the superior ulnar collateral branch arises. By careful dissection it was possible to preserve this branch as the involved segment of brachial artery with its aneurysm was excised. Following excision the radial pulse was faintly palpable. The concomitant vein was ligated and divided. Novocain block of the cervical sympathetic ganglia was done. The patient made an uneventful recovery and embarked for the United States on Dec. 30, 1944.

A.



B.

Fig 6 (Case 11)—A, Swelling of the flexor surface of the forearm due to false aneurysm of the radial artery. B, Photograph taken after dissection of the vascular lesion at operation. The gauze tape on the left supports the radial artery proximal to the false aneurysm while that on the right supports the same artery distally. Note the variation in diameter of the artery proximal to and distal to the aneurysm. The lowermost gauze tape retracts the median nerve while the silk sutures are placed around adjacent veins.

*False Aneurysm of the Brachial Artery in Association With Median Nerve Paralysis*

CASE 13.—A 25-year-old soldier had been struck in the left arm by artillery shell fragments on Feb. 28, 1945. Examination showed almost complete paralysis of the median nerve. At exploratory operation it was found that the median nerve was adherent to a pulsating mass which projected from the brachial artery. This aneurysm was only 4 mm. in diameter. The adventitia of the artery was successfully plicated over the aneurysmal bulge with five silk sutures. A small neuroma was excised from the median nerve. The patient was transferred to the United States on April 18, 1945. Function of the hand had improved remarkably.

*False Aneurysm of a Muscular Branch of the Femoral Artery Causing Exsanguinating External Hemorrhage*

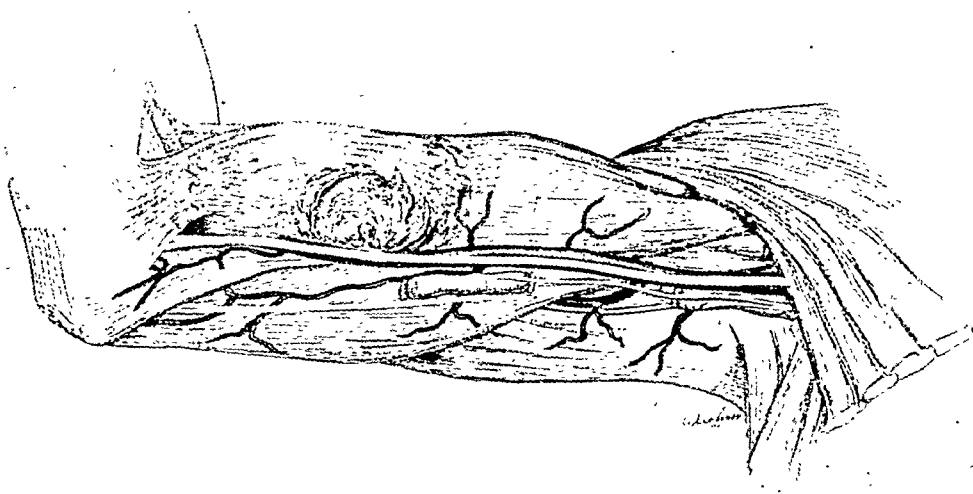
CASE 14.—An infantryman was injured in the left leg by enemy shell fragments on March 7, 1944. There was a deep wound of the soft tissues of the anteromedial aspect of the left thigh and there were compound fractures of the tibia and fibula on the same side. Débridement of the wounds was done at a medical regiment. It was stated in the record that at that time "a large clot was disturbed in the wound of the upper thigh causing profuse bleeding." The patient was admitted to this hospital with the leg in a plaster cast March 16. Inspection of the wounds of the lower leg showed that it was exuding gas bubbles and foul-smelling pus. *Clostridium welchii* was recovered. Incision and drainage were instituted. The wound of the upper thigh was not contaminated with *Cl. welchii*. On March 20 there was an exsanguinating hemorrhage from the wound of the upper thigh. Emergency exploration revealed that the source of the hemorrhage was a ruptured false aneurysm which arose from the muscular branch of the femoral artery which supplies the vastus medialis. The aneurysm was 2 cm. in diameter. The artery and the aneurysm were excised. The patient made an uneventful convalescence from both conditions and was transferred to another hospital on May 10, 1944.

*False Aneurysm of the Brachial Artery With Secondary Rupture and Formation of Adjacent Pulsating Hematoma; Partial Paralysis of the Median Nerve*

CASE 15.—A 27-year-old infantryman was struck in the left arm by mortar shell fragments while on a landing barge, Oct. 20, 1944. There was only slight hemorrhage from the wound. The soldier was admitted to this hospital on October 25. Examination showed that the left elbow was held at right angle flexion and there was a tense, expansile swelling of the lower third of the arm. A systolic bruit could be heard over this area. The degree of swelling is shown in Fig. 7, A. There were signs of impairment of function of the median nerve. The patient was kept in bed with the left arm in a sling. Despite these precautionary measures the patient experienced severe pain in the arm on November 10, twenty-one days after injury. Examination showed that the swelling of the lower arm had increased so that the tissues were quite tense. The angle of flexion at the elbow now had become acute. The radial and ulnar pulses were no longer present. The bruit had diminished in intensity. Ecchymosis of the tissues of the arm developed. At operation the dissection was made difficult by reason of the fact that, as the brachial artery was identified proximal to the lesion, the entire vascular tree of the arm went into vasospasm. The fascial sheath of the biceps brachii was distended by a tense mass and the tissues of the region were ecchymotic. The median nerve was adherent to this mass, which was limited anteriorly by the fascia of the biceps and inferiorly by the lacertus fibrosus. With gauze tapes securely placed around the artery proximally and distally, a tense hematoma measuring 8 by 6 cm. in size was broken into. Sixty cubic centimeters of clotted blood escaped, exposing a false aneurysmal sac 4 cm. in diameter. This had arisen from the brachial artery between the points at which the superior and the inferior ulnar collateral arteries arise. The opening into the brachial artery was 1 cm. in its greatest diameter. The pathologic picture is demonstrated in the artist's sketch shown in Fig. 7, B. This case would have been an excellent one for the Matas endo-



A.



B.

Fig. 7 (Case 15). A. Photograph showing the swelling of the lower third of the arm due to false aneurysm. The patient is holding the elbow in full active extension. This photograph was taken before the development of secondary swelling.

B. Artist's sketch showing the false aneurysm of the brachial artery which had ruptured to form a pulsating hematoma limited in its size by the fascial sheaths of the biceps brachii and the lacertus fibrosus. Note that the false aneurysm arises from the artery at a point midway between the points of origin of the superior and inferior ulnar collateral branches. The sac of the false aneurysm although thin was well formed and its lining showed circular striations, an effect of the whirlpool of blood within it.

aneurysmorrhaphy but since heparin was not available, the entire arterial segment between the superior ulnar collateral and the inferior ulnar collateral was excised. The concomitant vein was ligated and divided. At the close of the operation, the hand was cold though its color was good. Injection of novocain into the stellate ganglion was followed by return of warmth to the hand. The patient made an uneventful convalescence and was transferred to the United States on Dec. 16, 1944.

The interesting feature of this case was that the secondary hemorrhage from rupture of the false aneurysm occurred while the patient was at rest in bed with the affected arm in a sling.

*False Aneurysm of the Brachial Artery With Associated Paralysis of the Median Nerve*

CASE 16.—A 19-year-old paratrooper was wounded in the right arm by a fragment of mortar shell, Feb. 5, 1945. The missile entered the medial aspect of the lower third of the arm and lodged in the muscular tissue of the biceps. There was only slight hemorrhage from the wound of entrance. Early treatment was given at a station hospital. The diagnosis of pulsating hematoma was made at this hospital at the time of admission sixteen days after injury. During the next three days the systolic bruit over the lower arm became more intense and the diagnosis was changed to false aneurysm. There was almost complete paralysis of the median nerve. The radial pulse was palpable. The resting pulse rate, which had been 76 per minute, rose sharply to 90 on February 27 as the patient complained of constant pain in the lower arm. Fig. 8 is the photograph taken on that date. The bruit became less intense

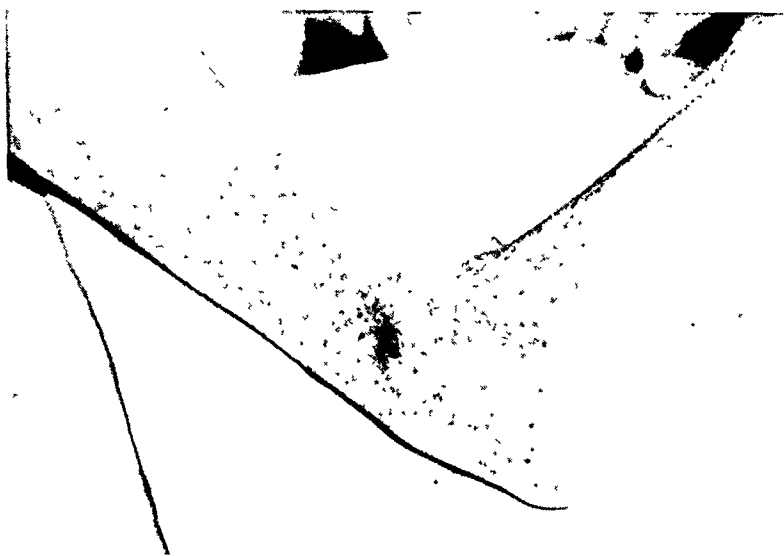


Fig. 8 (Case 16).—False aneurysm of the lower third of the brachial artery with secondary swelling due to second episode of hemorrhage. The elbow is held in right-angle flexion. Note the bulge of the granulating wound at the point of entrance of the shell fragment.

following this new episode of pain. The granulating wound at the point of entrance of the missile bulged progressively and flexion deformity of the elbow became more marked during the next forty-eight hours. Because the radial pulse was obliterated by the swelling it was necessary to explore the arm at operation on March 1. The pulsating mass proved to be a false aneurysm of the brachial artery which contained four ounces of blood and blood clot. After securing the artery proximally and distally with tape, the thin-walled sac was entered. The aperture in the brachial artery was a tangential opening 2.5 mm. in length and 1 mm. in width. As in Case 15, the tear was in the segment of brachial artery between the

superior and inferior ulnar collateral branches. This segment of artery was excised and a neurolysis of the median nerve was done. The concomitant vein was ligated and divided. The patient was transferred to a hospital in the United States, April 1, 1945, and made an uneventful convalescence.

Interest centers in the parallelism between the sequence of events in this case and in Case 15. In the latter, the secondary rupture of a false aneurysm of the same artery at the same level had occurred twenty-one days after injury while the patient was at rest in bed with the arm supported in a sling. In this case the circumstances were identical except that the epistaxis and secondary hemorrhage occurred on the twenty-second day after injury.

*Pulsating Hematoma of Brachial Artery*  
*Pulsating Hematoma; Pseudoaneurysm*

CASE 17.—A 27-year-old male patient whose physical findings which were very similar to those in Case 15, was injured by a machine gun bullet on Jan. 29, 1944, which entered the medial aspect of the lower arm and lodged in the soft tissue. There was a faint systolic bruit over the swelling.

*Formation of Secondary Hematoma*

and physical findings which were very similar to those in Case 15, were caused by a .31 caliber enemy machine gun bullet which entered the medial aspect of the lower third of the arm and lodged in the soft tissue. There was a faint systolic bruit over the swelling.

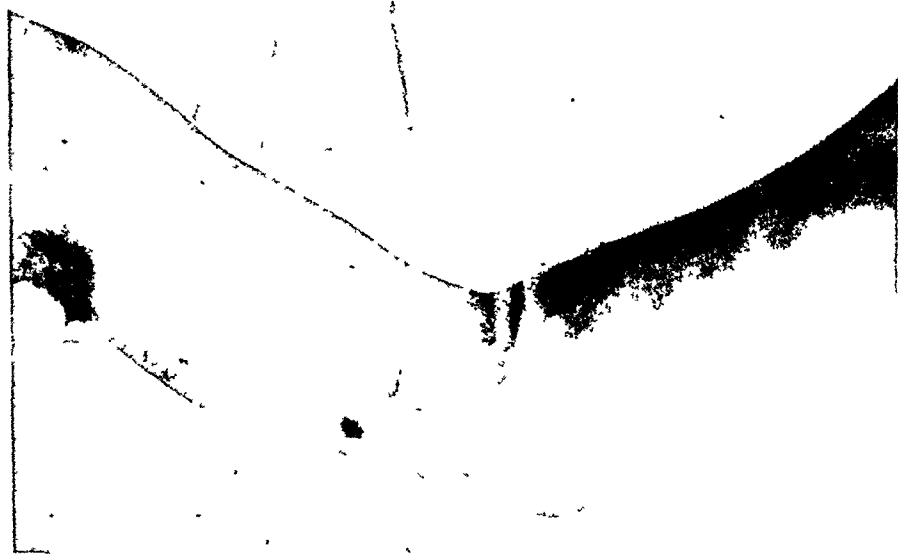


Fig. 9 (Case 17)—Photograph showing swelling of the antecubital fossa due to pulsating hematoma arising from the lowermost segment of the brachial artery. Note the dimpled scar on the medial aspect of the arm. This represents the point of entrance of the missile. The elbow is limited in extension to an angle of 110 degrees.

again there were signs of sensory and motor dysfunction of the median nerve and the angle of greatest extension at the elbow was 110 degrees. Compression of the pulsating, firm mass caused obliteration of the radial and ulnar pulses. This patient was conscious of the pulsation in the region of the elbow. On February 23, twenty five days after injury, the patient complained of pain and increased swelling over the lower arm. The pulse rate jumped from 72 to 88. This occurred while the patient was at rest in bed. The swelling increased progressively until February 26, when, because of the tautness of the swelling and sudden obliteration of the radial and ulnar pulses, it was necessary to explore the arm. At opera-

tion a double pulsating hematoma was exposed. Approximately one-half of the wall of the artery had been destroyed through a distance of 2 cm. The distal margin of the tear was only 4 mm. proximal to the bifurcation of the brachial artery into its radial and ulnar branches. A recent blood clot was broken into and two ounces of tightly packed clot were removed from a thin fibrous cavity limited by the muscle planes of the lacertus fibrosus and the biceps brachii. In the floor of this fibrous cavity there was a defect 1 cm. in diameter. This was plugged by organized clot around which bright red blood escaped. This cavity was opened into and found to measure 5 by 3 cm. in size. One and one-half ounces of organized blood clot were removed, closing the tear in the brachial artery as described previously. The involved segment of . . . was excised and neurolysis of the adherent median nerve was done. The concomitant vein . . . divided. At the time of transfer to a hospital in the United States on March . . . healed and there . . . some evidence of returning function of the median n . . . structure of the . . . still present.

The striking similarity . . . that . . . cases 15 and 16 emphasizes the great danger of . . . these aneurysms. In all three of these cases the secondary he . . . between the twenty-first and twenty-fifth day after injury. In . . . danger of gangrene of the arm following the episodes of secondary . . . ge.

*Pulsating Hematoma of the Posterior Tibial Artery With Rupture and Formation of Secondary Hematoma; Paralysis of the Posterior Tibial Nerve*

CASE 18.—A 21-year-old infantryman was struck by a missile from an enemy .31 caliber machine gun in the left leg below the knee on March 27, 1945. The missile entered the anterolateral aspect of the leg just inferior to and anterior to the head of the fibula. Its course was posteriorly and medially to lodge in the subcutaneous tissues of the posteromedial aspect of the upper third of the leg. At a battalion aid station, the foreign body was removed through an incision posteriorly. The patient was given sulfanilamide dressings and penicillin therapy was started. There was only slight hemorrhage from the wound of entrance. Débridement was not done. The diagnosis of pulsating hematoma was not made until April 16, the date of admission to this hospital. At that time the wound of entrance presented a sinus 5 cm. deep. The incision for removal of the foreign body had healed. There was a pulsating swelling which seemed to be in the muscles of the calf and also between the tibia and fibula. A distant systolic bruit could be heard over the posterior aspect of the calf. The dorsalis pedis and posterior tibial pulses were of full volume. There was anesthesia of the sole of the foot and the patient was unable to plantar flex the foot or toes. Attention was directed toward healing of the wound of entrance. The patient was kept at rest in bed. Gradually the wound of entrance filled in with granulation tissue and epithelized. On May 15, a medical officer, using a hemostat, inadvertently explored the thinly epithelized area representing the point of entrance of the missile. The patient suddenly complained of increased swelling in the calf and of pain about this area. There was blood tinged drainage from the thin epithelium over the point of entrance. Appearance at this time is shown in Fig. 10. Following this episode the dorsalis pedis and posterior tibial pulses were absent. Because of the danger of gangrene of the leg, surgical exploration was carried out on May 16. Consideration was given to the fact that the pulsating hematoma might have had its origin from partial tears of both the anterior and the posterior tibial arteries. The path of the missile was such that both vessels might have been damaged. The bruit was heard only over the posterior aspect of the calf while the maximal swelling was on the anterolateral aspect of the calf anterior to the head of the fibula at which point the missile had entered. The popliteal space and the calf were explored through an L-shaped incision. The two heads of the gastrocnemius were separated and the soleus was divided vertically. The popliteal artery and vein were identified. The posterior tibial artery was identified and secured with a gauze tape above and below the expansile, pulsating swelling which was between the soleus and the tibialis



posticus muscles. As the posterior tibial nerve was dissected free from the fibrous wall of the hematoma, it was found that two-thirds of its diameter had been destroyed through a distance of 2 cm. The hematoma was then evacuated. In this case the old blood clot could not be distinguished from the more recent formation. The clot was tightly packed in a cavity between the gastrocnemius and soleus muscles. It extended along the tract of the missile,

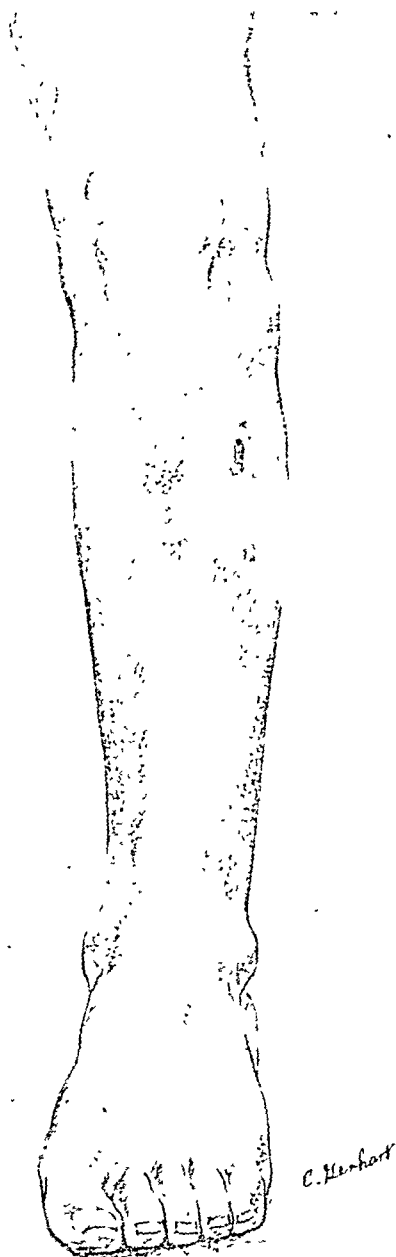


Fig. 10 (Case 18).—Artist's sketch showing the swelling of the upper leg due to pulsating hematoma secondary to injury of the posterior tibial artery. In this case there was a spontaneous secondary hemorrhage on the nineteenth day after injury. The hematoma expanded in the direction of the path of the missile causing the appearance of blood-tinged drainage from the thin epithelium over the point of entrance of the missile.

through the interosseous membrane to cause swelling near the point of entrance of the missile anteriorly. The cavity measured approximately 6 by 6 by 7 cm. in size, and from it seven ounces of clotted blood were removed. The injury to the posterior tibial artery presented as a tangential tear with destruction of one-half of the substance of the wall through a distance of 1 cm. between the retracted margins of the vessel. The involved segment of artery was excised. The posterior tibial vein was ligated and divided. The wound was closed without drainage. Following operation the dorsalis pedis pulse was present but the posterior tibial pulse was absent. Novocain block of the lumbar sympathetic ganglia on the affected side was done. The color and the circulation of the foot were normal on June 5, when the patient was transferred to the United States.

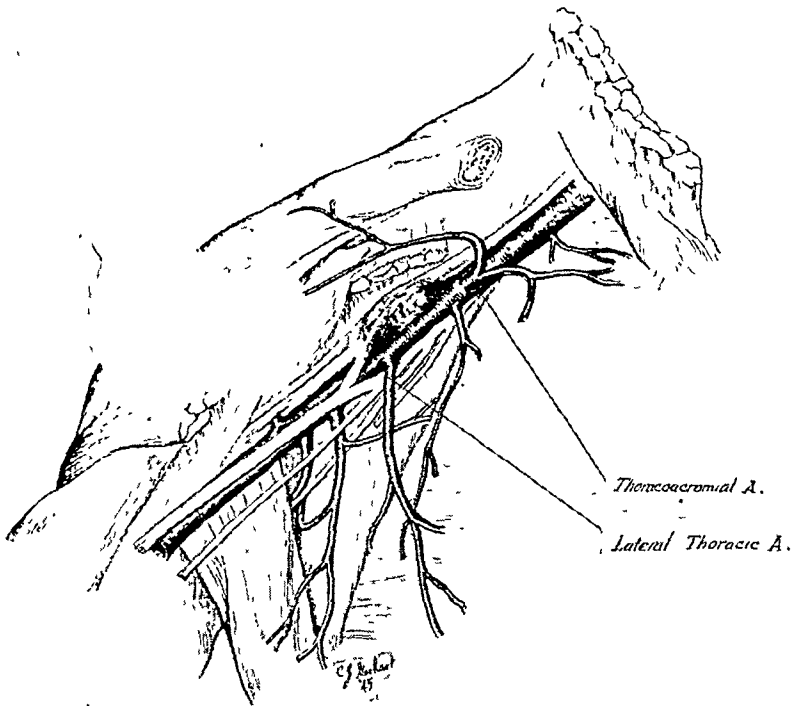


Fig. 11 (Case 19).—Sketch showing the location of this pulsating hematoma due to a partial tear of the second portion of the axillary artery. There were signs of incomplete paralysis of the brachial plexus. The extent of the hematoma was limited by the constricting brachial plexus. It was possible in this case to preserve the lateral thoracic and thoracoacromial branches at the time of excision of the involved segment of axillary artery.

*Pulsating Hematoma of the Second Portion of the Axillary Artery; Partial Paralysis of the Brachial Plexus*

CASE 19.—A 19-year-old infantryman was struck in the left shoulder posteriorly by a .25 caliber Japanese sniper's bullet on Oct. 20, 1944. The missile made its exit from a point just inferior to the lateral third of the left clavicle. His complaints were of inability to extend his wrist and of weakness of the forearm musculature. There was no primary débridement of the wounds. The diagnosis of pulsating hematoma was established at the time of admission to this hospital, October 27. There was fullness in the left infraclavicular area and a faint systolic murmur could be heard at this joint. The brachial, radial, and ulnar pulses were palpable and equal on the two sides. The blood pressure was recorded at 135/80 and was equal in the two arms. Pressure on the infraclavicular area caused obliteration of the brachial, radial, and ulnar pulses. There was an irregular area of anesthesia over the

dorsum of the hand. A definite wrist drop was present. Vascular collateral was encouraged by compressing the subclavian artery against the first rib at regular intervals each day. Because of the persistent paralysis, the infraclavicular and axillary regions were explored through a curvilinear incision on December 13. The clavicle was divided and the two ends were retracted as shown in Fig. 11. Exposure of the brachial plexus revealed that there was dense scar involving all three cords just proximal to the point at which the lateral and median cords combine to form the median nerve. Over this area there was a mass of degenerated fat approximately 2 by 7 cm. in size. As the scar tissue was dissected away from the components of the brachial plexus it was apparent that this was a pulsating hematoma which had developed from a tear of the axillary artery. The hematoma had been limited in its extension by the pressure of the neurovascular bundle. As the dissection proceeded it was evident that there was no evidence of direct damage to any of the cords of the plexus but that the cords were flattened out by pressure from the pulsating hematoma. The axillary artery was exposed and secured with a piece of gauze tape just proximal to the point where the lateral thoracic artery joined and distal clot 2 cm. in diameter was removed. The artery was surrounded by the scar tissue and the section of the artery was closed. The opening in the wall of the axillary artery was closed by the artery wall. The arterial stump pulsed freely and the ends of the cutaneous nerves and the ganglia were blocked with novocain time on. The patient was discharged.

Interest in this case is centered in the question of the relation of the fibers of the neurovascular bundle to the axillary artery effected in the formation of the pulsating hematoma.

#### Pulsating Hematoma of the Axillary Artery

CASE 20. A 21-year-old aviator was injured to the left wrist by a .30 caliber machine gun bullet while he was using the weapon on April 6, 1945. Examination May 11 showed a pulsating swelling 2 cm. in diameter over the flexor surface of the ulnar side of the forearm just proximal to the ulnar styloid process. There was a faint systolic bruit over the mass. There was numbness and tingling in the little and ring fingers but motor power of the ulnar nerve was not impaired. At operation, May 11, it was found that the ulnar nerve was adherent to a fibrous mass 3 cm. in diameter which enclosed clotted blood. This had developed from a partial tear of the ulnar artery at a point just proximal to the volar carpal ligament. The opening in the artery was 3 mm. in diameter. Following excision of the involved segment of ulnar artery, both the proximal and distal stumps pulsed. The adjacent vein was ligated. At no time was the circulation to the hand impaired. This soldier made an uneventful convalescence.

It is considered significant that regional peripheral nerves were involved in the fibrous reaction about the vascular lesion in all ten cases. Moreover, there were peripheral signs of motor and sensory dysfunction of the involved nerves in all of the cases and in three of these there was evidence of progressive paralysis. This is in contrast to the group of arteriovenous fistulas in which only two of ten patients had associated impairment of function of peripheral nerves. Another contrast in the findings in these two groups of cases is that five of the false aneurysms and pulsating hematomas exhibited marked flexion deformities of the nearest joint while this complication occurred in only one of the ten arteriovenous fistulas. Close study of the pathology at the operating

table explains these differences. In the arteriovenous fistulas the tremendous force of the pressure of the circulating blood has an immediate outlet in the peripheral vascular bed of the venous system. Consequently, there is minimal fibrous reaction around such fistulas. However, in those patients in whom the artery is incompletely divided and there is no injury to a concomitant vein, the force of the blood pressure exerts itself in the direction of the tract of the missile. The musculature is damaged already by the missile. The subsequent clot formation, limited by the constricting confine- more adjacent fascial sheaths, sets up an inflammatory react in a splinting of the part, the nearest joint being held in th

In the five patients in whom there was the pulse rate varied from 80 to 90 beats per minute. Negative in the ten cases in this series. Compression obliteration of the proximal to the lesion. of constant pain the lesion th w is ing sensation. In Of the ten at dit or the rear w instituted in all of the cases of the false aneurysmal as possible ary to evacuate clot and then se the orn rial ation was carried out cessful athe nglia was done post- operatively in si is sions w ted in all patients and only two exhibi res it the release from this hospital. The average lapse en dates o and operation was thirty-eight day One of th was returned ay and nine were transferred to th United States, further physical th and rehabilitation.

#### SUMMARY

Report is made of experience with twenty cases of peripheral vascular lesions following war injuries. These cases constitute .49 per cent of 4,040 surgical battle casualties which were admitted to this general hospital from the campaigns on the Philippine Islands. There were ten cases of arteriovenous fistula, six cases of false aneurysm, and four cases of pulsating hematoma. It was a unique experience to observe several of these patients as the lesion developed from pulsating hematoma into false aneurysm. It was noted that the bruit over a pulsating hematoma is faint while that over a false aneurysm is relatively loud. The observation was made that the intensity of the bruit increases as the clot which forms soon after injury undergoes liquefaction. Hemorrhage from the wound was severe in only three of the patients with arteriovenous fistula and in only one with false aneurysm. Contracture of the joint nearest the vascular lesion was exhibited in only one of the arteriovenous fistulas, while five of those patients in whom there was incomplete arterial laceration developed regional flexion contracture soon after injury. This difference is explained by the findings at operation. The force of the arterial blood from an arteriovenous fistula is received in the peripheral venous system. In those patients in whom the artery is incompletely torn, the force of the arterial pressure expends itself

in the direction of the path of the missile. Subsequent clot formation in the region of damaged muscles is limited only by the confines of adjacent fascial sheaths. Inflammatory reaction is reflected in a splinting of the part, the nearest joint being held in flexion. Moreover, it has been observed that, at the time of secondary hemorrhage from a false aneurysm or a pulsating hematoma, there is severe pain and the ankylosing contracture deformity increases while the bruit becomes less intense.

Paralysis of peripheral nerves was noted in only two of ten patients with arteriovenous fistula, while this complication was present in all patients with false aneurysm and pulsating hematoma. Primary emphasis is placed upon the treatment of wounds and the development of a functional limb. Amputation was indicated in this general category of hemorrhage only in one case, in which life or the viability of the limb was imperiled by the development of a rapid, uncontrolled contracture of the limb.

Those who showed progressive external hemorrhage or demarcation of tissue required surgical intervention in one case. Secondary internal hemorrhage and development of a large, glassy type of pulsating hematoma developed in two cases of arteriovenous fistula, in two cases of false aneurysm, and in one case of pulsating hematoma. Elapse of time between dates of injury and of secondary hemorrhage in these seven cases averaged thirty-four days. Photographs of specimens of these examples of pulsating hematoma secondary to rupture of aneurysm are shown. The secondary hematomas have developed in a fascial plane, that is, in that in which the primary aneurysm had formed. Experience with these patients has demonstrated that rest in bed and ordinary measures for immobilization of an extremity such as a splint or sandbag do not insure against the complication of secondary hemorrhage. Three of the twenty wounded soldiers whose records are reported herein were transported to the United States for definitive surgery.

None of the fifteen patients who were operated upon in this hospital showed signs of peripheral nerve insufficiency following operation. Elapse of time between dates of injury and operation averaged sixty-four days in the cases of arteriovenous fistula, and thirty-eight days in the case of false aneurysm and pulsating hematoma. In eight cases frequent block of the regional sympathetic ganglia with novocain was used as an adjunct to surgical excision of the lesion.

# CAUSALGIA SECONDARY TO INJURY OF THE MAJOR PERIPHERAL NERVES

TREATMENT BY SYMPATHETOMY

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**B**URNING pain, the distal portion of an extremity following injury to a major peripheral nerve presented the same problem in World War II as it had in previous wars. Our experiences have indicated that this problem has not always been recognized, and on occasions there has been an unfortunate tendency to classify some of these patients as psychoneurotic. The pain closely follows the description given by Mitchell and associates in 1864 and designated by the term causalgia. The portion of this description of the signs and symptoms of causalgia is given because it is a classic in medical literature and little can be added. It is a clear, concise and complete portrayal of the clinical picture.

The quality of this pain is very various, but it never attacks the trunk, rarely the arm or thigh and no oftener the forearm or leg. Its favorite site is the foot or hand.

The great mass of sufferers described this pain as superficial, but others said it was also in the joints and deep in the palm. If it lasts long, it was referred to the skin alone.

Its intensity varies from the most trivial burning to a state of torture, which can hardly be predicted but which reacts on the whole organism, until the general health is seriously affected.

The part itself is not alone subject to an intense burning sensation but becomes exquisitely hyperesthetic so that a touch or a tap of the finger increases the pain. Exposure to the air is avoided by the patient with a care which seems absurd, and most of the bad cases keep the hand constantly wet, finding relief in the moisture rather than in the coolness of the application.

As the pain increases, the general sympathy becomes more marked. The temper changes and grows irritable, the face becomes anxious and has a look of weariness and suffering. The sleep is restless and the constitutional condition reacting on the wounded limb exasperates the hyperesthetic state so that the rattling of a newspaper, a breath of air, another's step across the ward, the vibrations caused by a military band, or the shock of the feet in walking give rise to increase of pain. At last the patient grows hysterical, if we may use the only term which covers the facts. He walks carefully, carries the limb tenderly with the normal hand, is tremulous, nervous, and has all kinds of expedients for lessening his pain.

The skin affected in these cases was deep red or mottled, or red and pale in patches. The epithelium appeared to have been partially lost, so that the cutis was exposed in places. The subcutaneous tissues were nearly always shrunken, and when the palm alone was attacked, the part so diseased seemed to be a little depressed

and firmer, and less elastic than common. In the fingers there were often cracks in the altered skin, and the integument presented of all the affected part was glassy, and shining as though it had been skillfully varnished.<sup>1</sup>

These are the fundamental symptoms and findings of the disease. Additional factors for accentuating the hyperesthetic state commonly found in modern life are the roar of an airplane, the whistle of a train or a boat, and gazing downward at high altitude.

Present-day observations tend to confirm the clinical description as given by Mitchell. The changes of the peripheral vascular mechanism of the involved extremities are variable. It has been found variable in the individual patient. The electrocardiogram shows both normal and abnormal changes. The roentgenogram shows both normal and abnormal changes. The histogenesis of the disease is probably only those factors which are more

The exact etiology of the disease is not known. The pain seems to be localized. There are various theories but they have not been fully worked out. There is no reason for their review.<sup>2-7</sup> Despite the lack of knowledge of the etiology of the pain we feel that it is due to an interruption of the sympathetic nerve supply to the extremities or abolishes the symptoms of the disease.

It cannot be denied that the emotional factor in the patient will activate the autonomic nervous system and may in turn activate the pain reaction. This factor may assume too prominent consideration in the treatment of causalgia. Although the clinical features of the disease are well known, the patient suffering from this disease continues to be treated in the hospitals with a diagnosis of severe psychoneurosis. Often treatment is accomplished with a diagnosis of hysterical blindness or hysterical deafness. The diagnosis of psychoneurosis remains as the primary diagnosis. A typical case may be cited in Case 1.

#### CASE 1. PSYCHONEUROSIS

CASE 1.—A 21-year-old private was admitted to the hospital on Jan. 24, 1944. The diagnosis was partial paralysis of the left sciatic nerve, cicatricial contracture of the left popliteal region, and severe psychoneurosis, mixed type, with hysterical, obsessive, and compulsive features.

He had been struck by shell fragments Aug. 8, 1944, which resulted in a severe lacerating wound of the left thigh. There was a profuse hemorrhage following the injury. He had the usual treatment for wounds of this type. When he regained consciousness he was aware of severe burning pain in the left foot, particularly in the plantar surface. There was complete motor paralysis of the left leg and foot. He complained bitterly of the persistent pain in the foot. Noises, jarring, vibrations, and touching dry objects with the hands caused paroxysms of pain. While using a washcloth on his hands he found some of the paroxysms of pain in the foot were diminished. He started holding a wet cloth in his hands continuously. He was evacuated from the combat area to the United States. Though there had been spontaneous return of function of the sciatic nerve, the pain was unimproved. Eighteen weeks after his injury he was seen by a psychiatrist because of the bizarre pain in the left foot and because he persisted in keeping the hands moist. The following opinion was given.

Dec. 15, 1944, this 21 year old white private was referred for neuropsychiatric examination and appraisal because of nervous and hysterical type mannerisms (holding wash-

cloth in hands and wringing it continuously). He was relevant and coherent through the interview. He was thought to be of limited intelligence, and when questioned about holding the moist cloth he stated that he realized that it was a habit and not a desirable one. . . . He stated that for some unknown reason this simple childish habit was of considerable comfort to him. He volunteered that he was gradually trying to hold the cloth less and less. . . . His childhood history revealed that even at that time he resorted to fettering. It is believed that a person with this patient's mentality might very easily regress to childhood pattern at time of stress such as encountered by the patient on the . . . was not examined from the neurologic standpoint because . . . was a ward officer that he was to be transferred to . . . center for . . . undoubtedly this man had a fixation requiring . . . prolonged . . . was not advisable at this time to attempt such . . . not . . . showed considerable improvement. Diagnosis was . . . sensitive, and compulsive fear, severe. He . . . Examination showed a partial paralysis of . . . of causalgia of the left foot.

On Jan. 29, 1945, two . . . done with a transient complete block was done with immediate . . . continued until the present. The washcloth was discarded. . . . and no unusual behavior has existed after that time

Prolonged delay . . . During this period . . . of particularly . . . tissues and periarticular . . . are relieved, prolonged . . . affected is necessary because . . . is primarily due . . .

The treatment for . . . at the site of injury . . . division of the involved . . . supply to the affected extremity. In . . . to find "trigger points" and have . . . effects of such points.<sup>3</sup>

It has been the opinion of some . . . have seen the disease at an early stage that treatment at the site of injury is preventive or beneficial.<sup>8</sup> It has been recommended that a meticulous débridement be done, all devitalized tissue removed, and the nerve repaired if grossly injured. If the accompanying artery has been irreparably damaged, the destroyed area should be excised. We have not seen patients with causalgia until several weeks following injury and can give no evaluation of local treatment at an early stage of the disease. However, we have been impressed with the small benefit derived from local procedures in the late phases of the disease. In fact, some patients have shown an exacerbation of symptoms following local operative procedures. A typical example of this is cited in Case 2.

CASE 2.—A 29-year old white man was admitted Feb. 13, 1945, transferred from another hospital. He had been struck in the left axilla by a rifle bullet Dec. 8, 1944. There was a simple penetrating wound with complete motor and sensory paralysis of the left arm,

sympathetic block was . . . a . . . sympathectomy . . . continued until the present. The . . . and no unusual behavior has

Disease has been a usual occurrence. . . . of disuse affect the extremity. This . . . the hand is involved. Atrophy of soft . . . prominent findings. Even after symptoms . . . regain the normal mobility of the part . . . changes from disuse. This, we believe . . . of the symptoms.

There have been of three types: (1) treatment and neurolysis, (2) complete . . . interruption of the sympathetic nerve . . . group of patients we have been unable . . . experience with elimination of the



forearm, and hand. Immediately after the injury he had severe burning pain in the left hand. The pain prevented all rest, and he lost 15 per cent of his weight. He was given some medication for pain which made it bearable. After about four weeks' time there was spontaneous subsidence but not complete disappearance of pain. On admission to this hospital the pain was no longer troublesome.

Neurologic examination showed complete paralysis of the ulnar, median, radial, and musculocutaneous nerves. The blood count, urine, and blood serology were within normal limits.

Twelve weeks after his injury an exploration of the nerves of the arm was done. The ulnar, radial, and musculocutaneous nerves were found to be completely divided and were repaired by end-to-end sutures. The lateral half of the median nerve was also found to be divided but the medial half of the nerve was only dissected from the surrounding scar tissue.

Immediately following the operation the severe burning pain in the palmar surface of the hand recurred. After ten days a procaine block of the sympathetic supply to the upper extremity was done. He had a complete relief of pain that lasted thirty-six hours; the pain then returned though in lesser severity. The patient preferred to await spontaneous resolution of pains rather than to have a dorsal sympathectomy. Four weeks after operation all pain had ceased.

When exploring the involved nerve in patients with causalgia, it is rare to find the nerve completely divided. Usually there is a neuroma at the site of injury and occasionally no grossly abnormal area. In only two patients of this group was the nerve completely divided. Others have observed that true causalgia can occur in a nerve that has been completely divided.<sup>2, 8</sup> Often the involved nerve show excellent contractile function but voluntary movement is grossly limited because of pain. Under such conditions one is loathe to section the nerve in order to obtain relief. In our exploration, the nerve has suffered such extensive damage that it is doubtful that effective function will be regained spontaneously, excision of the damaged segment and suture of the nerve will frequently provide relief from pain.

The interruption of the sympathetic nerve supply to the involved extremity has proved to be the most useful procedure for the relief of causalgia in this series of patients. Periarterial sympathectomy was formerly used extensively in attempting to interrupt completely the sympathetic supply to an extremity.<sup>2</sup> It has become definitely established that this method is only partially successful. Direct attack on the ganglia supplying the extremity has largely supplanted the arterial stripping methods. The two may be used in conjunction, although we have not found it necessary to do so.

Temporary interruption of the sympathetic supply by procaine block of the sympathetic ganglia to the involved extremity is first done.<sup>9, 10</sup> If relief is obtained for one-half to one hour, excision of the sympathetic supply to the extremity will also be effective. Two patients of this series have obtained permanent relief from a single procaine block but it has been our experience that repeated chemical blocks usually have not produced permanent relief. Surgical excision has been preferred to alcohol block. After experiencing the relief obtained, the patient is permitted to decide if he desires the operative procedure.

The usual methods of sympathectomy have been employed. A muscle-splitting extraperitoneal approach for removal of the second and third lumbar ganglia has been used for producing preganglionic sympathectomization of the lower extremity.<sup>11</sup> Recently a modification of the thoracolumbar operation described by Smithwick<sup>12</sup> for use in hypertension has been employed for a more complete sympathectomization of the thigh. The Smithwick procedure has been used for sympathectomization of the upper extremity.<sup>13, 14</sup> It has the advantage of being a preganglionic division, of producing permanent results, and eliminating the Horner's syndrome which is produced by some methods. It has been felt that it was not justified to increase the extent of the sympathectomy when the dorsal approach was completely adequate. There have been no serious postoperative complications.

Although the paroxysmal, peripheral pain is relieved by these methods, there is often a residual discomfort which is experienced by practically all peripheral nerve injuries. When the pain is relieved, voluntary movement is re-established and the necessary treatment can be given to return the extremity to a state of normal function.

During the past twelve months, sixty-seven patients have been admitted to the hospital with injury to the lower peripheral nerve and causalgia of sufficient severity to require treatment. The lower extremity has been involved in twenty-three patients. The seat of the lesion was in the distribution of the posterior tibial nerve in thirteen patients, in the median nerve in five patients, and in the ulnar nerve in five patients. This is not in agreement with other reported series.<sup>2, 15, 16</sup> Usually the lower extremity has been designated as affected until more careful questioning and evaluation has established pain of greatest severity to the peripheral distribution of a specific nerve. The time of onset of pain has varied. It may be concomitant with the injury or occur several weeks following the injury. The posterior tibial has often been involved at the time of operative procedures for intractable hemorrhage from the tibial vessels. Concomitant injury of the accompanying blood vessels has been apparent in many instances of the present series although in all probability many of the others had vascular injury that were not recognized due to an incomplete lesion and the excellent collateral circulation present in the patients of this age group.

Sympathectomization of the involved extremity has been done in thirty patients; in twenty-two for lower extremity and in eight for upper extremity involvement. Two additional patients have had only the area of injury sympathectomized and are not included in this report.

It has been necessary to reoperate on one patient to obtain a more complete sympathectomization of the lower extremity. In one instance removal of the first and second lumbar ganglia was done after removal of the third and fourth ganglia had been ineffective (Table I, Case III). Complete relief of pain in the affected extremity was obtained by the more extensive operation. It is now our relief that the operation should always be of sufficient extent to sympathectomize the area of the site of nerve injury as well as the area of maximum pain.

TABLE I. CAUSALGIA OF LOWER EXTREMITY

CASE NO.	DATE OF INJURY	SITE OF INJURY	PRELIMINARY TREATMENT	DATE & EXTENT OF SYMPATHECTOMY	RESULT
I	Aug. 1944	Buttocks	Neurolysis, lumbar block	Aug. 8-44 L-2, L-3	Failure
II	June	Thigh, proximal third	Lumbar block	Aug. 12-44 L-2, L-3	Excellent
III		Popliteal space	Neurolysis, lumbar block	Sept. 4-44 L-2, L-3	Good
IV		Thigh, middle third	Lumbar block	Sept. 4-44 L-3, L-4 Mar. 19-45 L-1, L-2	Failure Excellent
V	Aug.	Thigh, middle third	Lumbar block	Nov. 20-44 L-2, L-3	Good
VI		Leg, middle third	Lumbar block	Nov. 29-44 L-2, L-3	Excellent
VII		Thigh, middle third	Lumbar block	Jan. 11-45 L-1, L-2, L-3	Excellent
VIII		Leg, proximal third	Lumbar block	Jan. 17-45 L-2, L-3	Good
IX	C	Leg, middle third	Lumbar block	Jan. 22-45 L-2, L-3	Good
X	July	Thigh, proximal third	Lumbar block	Jan. 29-45 L-1, L-2, L-3	
XI	July	Leg, middle third	Neurolysis, lumbar block	Jan. 29-45 L-2, L-3	
XII	July	Thigh, proximal third	Lumbar block		
XIII	Aug. 8-44	Thigh, distal third	Lumbar block		Excellent
XIV	June 10-44	Thigh, middle third	Lumbar block	Feb. 1-45 L-2, L-3	Good
XV	12-44	Buttocks	Lumbar block	Feb. 5-45 L-2, L-3	Good
XVI	June 29-44	Thigh, proximal third	Lumbar block	Feb. 8-45 L-2, L-3	Good
XVII	Jul. 27-44	Thigh, middle third	Neurolysis, lumbar block	Mar. 2-45 L-2, L-3	Good
XVIII	Sept. 29-44	Leg, middle third	Lumbar block	April 13-45 L-2, L-3	Good
XIX	Dec. 27-44	Thigh, distal third	Lumbar block	May 14-45 L-2, L-3	Good
XX	Jan. 11-45	Thigh, distal third	Lumbar block	May 24-45 L-2, L-3	Good
	Mar. 4-45	Thigh, distal third	Lumbar block	June 4-45 L-2, L-3	Good
	44	Thigh, distal third	Lumbar block	June 20-45 L-2, L-3	Good

Results were judged by the relief of pain experienced and the ability to use the affected extremity. Results were good to excellent in twenty-eight patients (Tables I and II). Two patients of this series did not obtain relief by sympathectomy. Before the more complete operation was resorted to, a cordotomy was done in one patient, after removal of the second and third lumbar ganglia had failed to give relief of pain (Case I, Table I); the nerve injury was in the proximal third of the thigh and the site of injury had not been sympathectomized. The second failure had a completely technically satisfactory dorsal sympathectomy yet there was no relief of symptoms; we have no adequate explanation for the failure in this instance.

TABLE II. CAUSALGIA OF UPPER EXTREMITY

CASE NO.	DATE OF INJURY	SITE OF INJURY	PRELIMINARY TREATMENT	DATE & EXTENT OF SYMPATHECTOMY	RESULT
I	Aug. 8-44	Arm, proximal third	Neurolysis, dorsal block	Jan. 24-45 D-2, D-1	Excellent
II	Nov. 13-44	Arm, proximal third	Neurolysis, dorsal block	Feb. 1-45 D-2, D-1	Excellent
III	Dec. 15-44	Forearm, middle third	Dorsal block	Feb. 1-45 D-2, D-1	Excellent
IV	Nov. 26-44	Forearm, distal third	Dorsal block	Feb. 1-45 D-2, D-1	Good
V	Nov. 6-44	Clavicular region	Neurolysis, dorsal block	Feb. 1-45 D-2, D-1	Failure
VI	Feb. 8-44	Clavicular region	Dorsal block	June 1-45 D-2, D-1	Good
VII	Mar. 9-44	Axilla	Dorsal block	June 1-45 D-2, D-1	Excellent
VIII	Dec. 20-44	Arm, middle third	Neurolysis, dorsal block	June 1-45 D-2, D-1	Excellent

Not included in this group of patient with causalgia following major peripheral nerve injuries were three patients with burns in the lower extremities following cauda equina injuries. Lumbar sympathectomies have been performed in these patients with out benefit. The site of injury was not sympathetic and may have some bearing on the failure.

#### SUMMARY

1. Causalgia concomitant with injuries of the major peripheral nerves presented a real problem of management in World War II, as in preceding wars.
2. During the past year there have been sixty-seven patients with major peripheral nerve injuries and concomitant causalgia of sufficient severity to require treatment admitted to this hospital.
3. Thirty of this group desired sympathectomy after experiencing the relief obtained by sympathetic block.
4. Of this group twenty-two had lumbar sympathectomies and eight had preganglionic dorsal sympathectomies.
5. Good to excellent results were obtained in twenty-eight of the patients. Failure to relieve symptoms and re-establish use of the affected part occurred in two patients.
6. The sympathectomization should be of sufficient extent to include the area of injury as well as the area of symptoms.
7. Early sympathectomization of the affected extremity including the area of injury will, in the vast majority, relieve the symptoms of the disease and prevent the profound disabilities of disuse.

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# GUNSHOT WOUNDS OF THE ABDOMEN

## A REVIEW OF 149 CASES

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IN THIS paper is given an analysis of 149 gunshot wounds of the abdomen and gunshot wounds of the abdominal wall treated at Harlem Hospital over an eleven-year period, from 1933 to 1944. Thirty-five of these cases were included in a report by McGowan<sup>1</sup> in 1935. The high mortality of these injuries caused us to make this study and the relative paucity of reports on this subject made it seem worth while to record our experiences and what we have learned about the emergency handling of these cases. Most of the principles that we follow even at the present time were outlined by Connors<sup>2</sup> from this hospital in 1923 and amplified by the subsequent reports of Silleck,<sup>3</sup> Eisberg,<sup>4</sup> and McGowan. Their papers were reports of penetrating wounds of the abdomen in which gunshot wounds were combined with stab wounds. It is now generally agreed that because of the more serious character of gunshot wounds they should be studied separately.

Our series includes 115 penetrating gunshot wounds of the abdomen and 34 gunshot wounds of the abdominal wall. The patients in this series were treated by the surgeon who happened to be on duty at the time of the injury.

### INCIDENCE

Gunshot wounds in general are not as frequent in New York City as they are in some of our southern cities due to the fact that it is against the New York law to carry or have a pistol without a permit. Therefore, this series of cases is not as large as others that have been reported for the same period of time from cities where there is no such law.

All wounds in this series were inflicted by pistol bullets; we have had no experience with shotgun injuries.

It should also be pointed out that injuries of this character in civil life carry, as a rule, a higher mortality than that obtained in military life, because the average soldier is a more rugged physical specimen and reacts better physiologically, when injured, than the average large city civilian. It has been our experience, with the few soldiers whom we have treated, suffering from any type of trauma, that they have much greater powers of recuperation than other citizens.

### DIAGNOSIS

The diagnosis of gunshot wound or wounds of the abdomen is usually as simple as the injury is obvious. The chief point of interest to the surgeon

is whether or not there has been an intra-abdominal injury, and the decision for or against operation depends upon this. This decision is, at times, difficult to make. When there is the slightest doubt as to whether a blood vessel or a viscus within the abdomen is injured, the patient should be subjected to immediate exploratory laparotomy. Connors insisted upon careful inspection of the bullet wound and its direction and a decision as to whether it was one of entry or exit. If there are several wounds, it is important to know how many of these are of entry and how many of exit. The location of the incision is, in part, governed by this and is helpful in making a tentative diagnosis of visceral injury. The path of the bullet should be mentally visualized, if possible, by the surgeon at the time of operation. Palpation will indicate rigidity, tenderness, and rebound tenderness, which are signs of peritoneal irritation, and in cases where there is doubt as to whether or not the peritoneal cavity has been entered, they are of great diagnostic value. Oberhelman and Le Count<sup>5</sup> have pointed out that side-to-side injuries in the abdomen are the most serious; bullets entering from front to back are the next most serious; and those entering from the back are usually the least serious.

In Table I, it is of interest to note that 64.3 per cent of the patients with penetrating gunshot wounds of the abdominal wall had tenderness, 66.1 per cent had abdominal rigidity, while none of those with nonpenetrating wounds showed abdominal rigidity, only 11.7 per cent showed tenderness, and none showed vomiting.

TABLE I

TYPE OF GUNSHOT WOUND	NUMBER OF CASES	TENDERNESS		ABDOMINAL RIGIDITY		VOMITING	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Penetrating	115	74	64.3	76	66.1	5	4.3
Nonpenetrating	34	4	11.7	0	0	0	0

The percentage of cases with abdominal tenderness and abdominal spasm is lowered by the fact that seventeen patients were unconscious at the time of admission to the hospital, in profound shock, and with obvious penetrating gunshot wounds of the abdomen. Our percentage of patients with vomiting in penetrating gunshot wounds of the abdomen is only 4.3 per cent (five cases), whereas Hamilton and Duncan<sup>6</sup> reported vomiting in 46 per cent of their patients, while Storck<sup>7</sup> reported only three cases of nausea and vomiting in a series of forty-six cases.

The amount of abdominal tenderness and spasm is found to be in direct proportion to the amount of blood in the peritoneal cavity or to the amount of spillage from the gastrointestinal tract.

The passage of fresh blood by rectum, urethra, or mouth points to the injury of the lower bowel, urinary tract, or stomach, and immediate exploration is indicated in these cases regardless of other abdominal findings. In this series there were found the following figures: bleeding per rectum, 1 case; bleeding per urethra, 9 cases; and hematemesis, 2 cases.

## RADIOGRAPHIC FINDINGS

Röntgenologic study has helped us in these cases. Where there is no wound of exit of the bullet, a roentgenogram taken immediately with a portable x-ray machine at the time of admission will help locate the bullet and aid the surgeon in visualizing in his mind the path the bullet has taken; in some instances, if the patient is not in serious condition, free gas under the diaphragm, seen in the x-ray view of a patient sitting upright, is evidence of a perforation of the gastrointestinal tract. Occasionally this is the sole proof of perforation of a hollow viscus.

In Table II it is seen that the presence of gas under the diaphragm on x-ray examination is practically pathognomonic of intestinal tract perforation.

TABLE II. RADIOGRAPHIC FINDINGS IN TWENTY-TWO CASES

	NUMBER OF CASES	OPERATION
Pneumoperitoneum	15	Gastrointestinal tract perforation
Pneumoperitoneum absent	6	No perforation
Pneumoperitoneum absent	1	Two small perforations of the gastrointestinal tract

## ABDOMINAL TAP

In difficult cases, as a diagnostic aid, we have also used abdominal tap. Peritoneal tap, using a spinal puncture needle, is performed in all four abdominal quadrants. In this series of cases, eight abdominal taps were performed; in five cases, the tap was positive with blood being obtained. At operation in these five cases, free blood was found in the peritoneal cavity. In three cases the abdominal tap was negative and no free fluid or perforation of the intestinal tract was found. A negative abdominal tap does not mean that there can be no intra-abdominal injury, but it is reasonably certain that a massive intra-abdominal hemorrhage will be diagnosed by peritoneal tap if the abdominal puncture is properly performed. Dixon, Martin, and Ochsner<sup>8</sup> have recently recommended abdominal tap as helpful.

In Table III are listed the reports of the authors having the largest series of cases, with their operative findings, together with our own.

The age incidence is indicated in Table IV; this reveals that the mortality is definitely higher after the age of 31 years. Hamilton and Duncan also observed that the mortality rate is higher in gunshot wounds of the abdomen

TABLE III

AUTHOR	NUMBER OF CASES	OPERATIVE MORTALITY (PER CENT)
Oberhelman and Le Count	301	61.4
Rippy	292	61.9
Hamilton and Duncan	182	48.9
Taylor	101	60.0
Elkin and Ward (pistol and rifle wounds)	176	47.7
Wilkinson, Wright, and Hill	115	60.0

In Elkin and Ward's series of 176 penetrating wounds, there were seven cases in which no perforations were found.



is whether or not there has been an intra-abdominal injury, and the decision for or against operation depends upon this. This decision is, at times, difficult to make. When there is the slightest doubt as to whether a blood vessel or a viscus within the abdomen is injured, the patient should be subjected to immediate exploratory laparotomy. Connors insisted upon careful inspection of the bullet wound and its direction and a decision as to whether it was one of entry or exit. If there are several wounds, it is important to know how many of these are of entry and how many of exit. The location of the incision is, in part, governed by this and is helpful in making a tentative diagnosis of visceral injury. The path of the bullet should be mentally visualized, if possible, by the surgeon at the time of operation. Palpation will indicate rigidity, tenderness, and rebound tenderness, which are signs of peritoneal irritation, and in cases where there is doubt as to whether or not the peritoneal cavity has been entered, they are of great diagnostic value. Oberhelman and Le Count<sup>5</sup> have pointed out that side-to-side injuries in the abdomen are the most serious; bullets entering from front to back are the next most serious; and those entering from the back are usually the least serious.

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occurred within the first twenty-four hours. In thirty-four cases the systolic pressure on admission was 170 mm. of Hg and in forty cases the blood pressure, systolic, was 70 mm. of Hg or lower. All patients should receive anti-tetanic serum and antigas gangrene antitoxin upon admission. Most delay before transfusion is caused by the time it takes to determine the patient's blood type.

#### ANESTHESIA

We used open cone ether in all of our cases and found it to be the most satisfactory type of anesthesia. Spinal anesthesia is to be condemned because it increases shock and increases spill of intestinal content. The type of incision used depends upon the point of entrance and the probable path of the bullet. Too much emphasis cannot be placed upon the greatest speed possible in operating compatible with good, careful surgery. Connors, Eisberg, and McGowan have pointed out the need for incisions of adequate length and evisceration if there is difficulty in exposing the lesion. The method of examination advocated by Elkin and Ward<sup>10</sup> is excellent, that is, the cecum is examined first; the small intestine is then inspected throughout its length up to the ligament of Treitz, and any perforations are closed when found; the large intestine is explored next; then the stomach and retroperitoneal structures are examined. Each surgeon usually explores the abdomen according to his own method.

Table VII shows that the frequency of injury is, in the main, in proportion to the space occupied by the viscus within the peritoneal cavity.

TABLE VII. INJURIES TO ABDOMINAL VISCERA

Small intestine	47
Large intestine	37
Stomach	30
Liver	27
Diaphragm	12
Mesentery	10
Omentum	8
Urinary bladder	6
Kidney	5
Spleen	6
Gall bladder	3
Pancreas	1

TABLE VIII. ASSOCIATED INJURIES—BULLET WOUNDS

Extremities	32
Lower	20
Upper	12
Chest, penetrating	14
Head	4
Neck	2
Buttock	2
Mandible	1
Penis	1
Scrotum	1
Fractured rib with chest	1
Spine with chest	1
Total	59

This group of cases had an exceptionally large number of associated injuries; in fact, 59 of the 149 cases had associated extra-abdominal injuries. This, of course, has a very direct bearing on mortality and plan of treatment.

In Table IX is shown the mortality in relation to associated injuries.

TABLE IX. MORTALITY WITH AND WITHOUT ASSOCIATED INJURIES

PERFORATION OR LACERATION OF	LIVED	DIED	MORTALITY (PER CENT)
Small intestine	7	7	50.0
Small intestine with associated injuries	8	25	75.7
Stomach	3	4	57.1
Stomach with associated injuries	4	19	82.6
Liver	5	2	28.5
Liver with associated injuries	6	14	70.0
Large intestine	3	5	62.5
Large intestine with associated injuries	6	23	79.3
Diaphragm	0	0	0.0
Diaphragm with associated injuries	2	10	83.3
Urinary bladder	3	0	0.0
Urinary bladder with associated injuries	0	3	100.0
Kidney	2	0	0.0
Kidney with associated injuries	1	2	66.6
Spleen	1	0	0.0
Spleen with associated injuries	2	3	60.0

The mortality rate for perforation of any single viscus is highest in perforation of the large bowel. In this series, as is shown in Table IX, there were eight perforations of the large intestine alone and there were five deaths, which gives a mortality of 62.5 per cent. There were a total number of twenty-nine cases of perforation of the large bowel with associated injuries and in this group the mortality rate was 79.3 per cent. It should also be pointed out that it is relatively unusual to have a perforation solely of the large bowel, because when there is large bowel injury usually some associated lesion exists. The high mortality rate in perforation of the large intestine is due to the higher bacterial count found at this level of the intestine and the spillage into the peritoneal cavity in most cases leads to a peritonitis which is often fatal. In the transverse colon and in the sigmoid, exteriorization of the intestine, in our opinion, is of value. Hamilton and Duncan observed that there was a progressive increase in mortality from peritonitis as the level of the perforated bowel descends from jejunum to colon. However, Storek reported in his series of cases a relatively low mortality in colonic injuries and stated that it was due probably to the relatively small quantity of spillage which ordinarily accompanies such injuries. It has been our experience that sulfonamides placed in the peritoneal cavity at the time of operation, and followed by sulfonamides by mouth or intravenously, have not reduced the mortality rate in these cases. This is contrary to the published reports of others. We use sulfonamides routinely and will continue to do so, but it just happens that our results to date with their use have not been as impressive as the results reported by other clinics.

Perforations of the stomach show a mortality rate of 57.1 per cent, while perforations of the stomach plus associated injuries give a mortality rate of

82.6 per cent. Rippey found his mortality rate for stomach injuries alone to be 53.3 per cent and in his cases where the stomach injury was associated with another lesion the mortality rate was 65.2 per cent. Hamilton and Duncan pointed out that perforation of the stomach and duodenum gives a rather high mortality rate because of the relatively large associated blood loss, the difficulty of exposure, and often the frequency of associated thoracic injury. Our study is in agreement with these quoted authors and we also found that there was a higher incidence of postoperative pneumonia in patients with stomach perforation than in any other group. Perforation of the small intestine had the lowest mortality rate of any segment of the gastrointestinal tract, which was 50 per cent for perforation of the small bowel alone and 75.7 per cent where there were associated injuries.

The mortality rate in patients with chest and coincidental abdominal injuries was 83.3 per cent. This is in striking contrast to those admitted to the hospital with a perforated injury of the chest alone, as the majority of these patients recovered on a conservative regime. Hardt and Seed<sup>11</sup> reported a mortality of 56 per cent. Injuries to the liver gave a mortality rate of 28.5 per cent and injuries of the liver plus associated injuries gave a mortality rate of 70 per cent. We had twenty-seven cases of liver injuries with sixteen deaths and three of the patients exhibited the symptoms that go with the so-called "liver death." The syndrome of "liver death," as described by Heyd,<sup>12</sup> is characterized by high temperature, falling blood pressure, circulatory collapse, coma, and then death. The blood loss in these three cases was insufficient to produce the symptoms that we found.

It was pointed out by Oberhelman and LeCount that the number of perforations of a hollow viscus has a direct bearing on mortality. This is confirmed by us, as shown in Table X. Of the 104 patients operated on, 43 lived, 61 died, and 12 of these 61 had associated injuries of head, neck, chest, or extremities.

TABLE X. DIFFERENTIAL MORTALITY IN RELATION TO NUMBER OF PERFORATIONS OF GASTROINTESTINAL TRACT

NUMBER OF PERFORATIONS OF GASTROINTESTINAL TRACT	DIED	LIVED	MORTALITY (PER CENT)
1	12	11	52.2
2	18	11	62.1
3	10	3	76.9
4	2	4	33.3
5	2	0	100.0
6	2	0	100.0
7	2	0	100.0
8	5	1	83.3
9	1	1	50.0
11	1	1	50.0
12	1	1	50.0
13	1	0	100.0
15	1	0	100.0
16	1	0	100.0
Total	59	33	

POSTOPERATIVE COMPLICATIONS

Hemorrhage and shock are the most common postoperative complications. Following operation, after hemorrhage has been controlled, postoperative shock is superimposed upon the shock and hemorrhage due to the original injury. In the 115 penetrating wounds, 74 patients entered in shock; 57 died, which gave a mortality rate of 77.03 per cent, as shown in Table V. It is noted that 52.4 per cent of all operative deaths occurred within the first four hours, which indicates the importance of shock as a death-producing factor. The other complications occurring in this series are tabulated in Table XI. The mortality rate for these complications is 50 per cent.

COMPLICATIONS		MORTALITY	
Clinical peritonitis	12	6	50.0
Pneumonia	7	4	57.1
Evisceration	1	1	100.0
Subphrenic abscess	1	1	100.0
Infected retroperitoneal hematoma	1	1	100.0
Intestinal obstruction due to adhesions	1	1	100.0

Twelve patients developed clinical complications, of these were patients that had come to the hospital in shock, as shown in Table XI, seven recovered. In one it occurred on the fourteenth day, in another it developed pneumonia on the fourth day. The complications were preceded by a serosanguineous discharge. The percentage of evisceration was 2.9, as obtained by Hamilton and Duncan and Taylor. This is slightly higher than the occurrence of evisceration in general, which is placed usually between 1 and 2 per cent. One patient developed a subphrenic abscess due to a perforation of the small intestine (eight perforations) on the fourth day. The patient died on the sixth day after drainage. A retroperitoneal hematoma became infected on the fourth day. This was incised and a large abscess cavity was found containing 800 c.c. of thin, yellowish pus with a foul odor. The cavity almost to the costal margin in the posterior axillary line to the internal abdominal ring and posteriorly to the border of the rectus spinus muscles. The patient made an uneven recovery and was discharged on the sixteenth postoperative day. One patient developed postoperative adhesions with resultant intestinal obstruction and was operated upon on the thirty-third day following the first operation (there were two perforations of the jejunum about six inches below the ligament of Treitz). In the second operation there were numerous fine and moderately firm adhesions matting the intestines together on the left side of the abdomen. This patient died on the sixth day following operation.

## POST-MORTEM FINDINGS

Excepting for the splendid detailed report of Oberhelman and Le Count, too few of the recent excellent articles on this subject from the larger clinics have given in detail the post-mortem findings in the fatal cases. This we consider very important.

Post-mortem examinations were made on all of the patients who died in this series. The medical examiners of New York City, and the following reports were made available to us for study:

In Table XIII the cause of death in each case is listed and the post-mortem findings are given in detail.

CASE NO.	TIME OF DEATH	POST-MORTEM EXAMINATION	
		CAUSE OF DEATH	POST-MORTEM FINDINGS
1	4		5
2	30 min.		4
3	11		1
4			1

## TO BE STARTED

the following cases in which the patient died because of death was hemorrhage and a blood vessel, as shown in Table XIII. In all cases hemorrhage due to gunshot wound of the peritoneum. This only emphasizes

## PATIENTS WHO DIED BEFORE OPERATION

## AUTOPSY FINDINGS

CASE NO.	TIME	POST-MORTEM FINDINGS
1	4	Peritonitis; bullet wound of liver 1000 c.c. of blood in right pleural cavity and 300 c.c. in the peritoneal cavity
2	30 min.	Bullet wound of right lung, inferior vena cava, ex-
3	11	Peritonitis; 8 perforations of small intestine
4		Hemoperitoneum; 500 c.c. of blood in right
5		Right diaphragm, and anterior and posterior
6		walls of stomach; 300 c.c. of blood in peritoneal cavity and 1,300
7		c.c. of blood in right pleural cavity
8		Perforation of right common iliac vein and artery, perforation of
9		the ileum 8 inches from the ligament of Treitz and 2 perfora-
10	30 min.	Laceration of abdominal aorta, hepatic artery and vein, left renal
11		vein, and left kidney
12		Laceration of left subhepatic vein, hemoperitoneum; 12 perforations
13	2 hr.	of the jejunum
14		Hemoperitoneum; 10 through-and-through perforations of the jeju-
15	15 min.	num
16		Complete severance of abdominal aorta, inferior vena cava; duode-
17	15 min.	num completely severed, perforation of the liver
18		Bullet wound of left external iliac artery and vein, through-and-
19		through perforation of the rectum, 12 perforations of the small
20		intestine

\*Through the courtesy of Dr. Thomas A. Gonzales, Chief Medical Examiner.

the fact that the greater the degree of shock the greater the indication for immediate operation so that hemorrhage can be controlled.

#### LESIONS MISSED AT OPERATION

uses in which the lesions of importance were missed by the operation is outlined in Table XIV.

TABLE XIV. LESIONS OVERLOOKED AT OPERATION

CASE NO.	POSTOPERATIVE DAY OF DEATH	MISSED LESION FOUND AT AUTOPSY	CAUSE OF DEATH
1	9th	Perforation through-and-through of the lower portion of the rectum; patient developed a peritoneal phlegmon	Peritonitis
2	4th	Perforation of the ascending colon 10 inches above the ileocecal junction measuring $\frac{5}{8}$ and $\frac{1}{4}$ inch in diameter	Peritonitis
3	6th	Perforation of the pericardium	Pericarditis
4	2nd	Two perforations in the descending colon near the splenic flexure	Peritonitis
5	9th	Perforation of the duodenum near its pancreatic border about $\frac{1}{2}$ inch in length, and a through-and-through perforation of the stomach 3 inches from the pylorus	Peritonitis
6	1st	Two perforations of the stomach: one in the duodenum, the other in the body	anesthesia
7	1st	Laceration of the spleen	
8	2nd	Small perforation of the aorta at the vertebra	derwater
9	1st	Perforation of the iliac vein	postoperative
10	1st	Two lacerations of the iliac vein	day

Five perforations of the gastrointestinal tract were not missed by the surgeon. There were three lacerations of the major blood vessels missed by the surgeon. There was one laceration of the spleen found and one of the pericardium. Of the missed perforations of the intestinal tract, two were of the duodenum, one of the ascending colon, one of the descending colon, and one of the rectum. From Tables XIII and XIV it is to be noted that injuries to major blood vessels are not infrequent and are a cause of very rapid death.

In this series there were, therefore, ten cases in the series where a fatal injury was missed at the time of operation, or in 13.8 per cent of the cases. It is important to realize that speed must not be at the expense of care, and, too, that every surgeon in the handling of these cases should develop a plan of investigation at the time of operation that will not permit of the possibility of overlooking a serious injury except under bizarre circumstances. The exploration should be done with great care, speed, and thoroughness. It has been our feeling that most missed lesions were the result of incisions that were too short and did not permit of sufficient visualization.

#### COMBINED THORACIC AND ABDOMINAL INJURIES

In thoraco-abdominal injuries the bullet wound of entrance is, in the majority of instances, in the chest. In only one case out of fourteen was there a

lesion found within the chest where the wound of entrance was solely to be found in the abdominal wall. In nine cases out of the for the bullet wound of entrance was in the chest and penetrated to the . This is explained by the fact that the patient was in a bending or n at the time of injury. It is therefore wise for surgeons when chest injuries to keep in mind the possibility of a concomitant i lesion.

In Table XV there are listed the data on twelve f es . raco-abdominal wounds.

In this series there were three fatal cases of combined abdominal and head injuries. In one case the patient was unconscious on admission and presented a bullet wound of entrance in the left upper quadrant one inch below the costal margin and a bullet wound of the left temporal region of the skull; he died one hour after admission to the hospital. In another case the patient showed bullet wounds in the anterior portion of the temporal region, but x-ray of the skull was negative for fracture, and one wound of the right lower quadrant.

At operation four perforations of the ileum and one of the cecum were found. patient . . . with postoperative day. The third patient showed a . . . region and of the chest, the third inter- . . . at operation he showed a per- . . . and died on the first post-

abdominal wounds . . . explored promptly, but opinion . . . the advisability of . . . g operation to treat shock. The . . . Hospital is to determine the patient's blood type at once and . . . ous infusion of normal saline solution immediately, continuing . . . available and then substituting blood for the normal saline . . . and Rippey advise against operating, if possible, until the . . . pressure has risen above a critical level. We recommend imme- . . . irrespective of the condition of the patient, because we feel that . . . hemorrhage is a most important factor in the treatment of co- . . . ntinuing shock. Hamilton and Duncan also take this view. Anti-

shock . . . res should be continued along with surgical intervention. Wangen- . . . steen solution for decompression is used routinely in all abdominal operations and the tube is passed immediately after the patient has arrived at the hospital. Sulfanilamide, 10 Gm., is placed in the peritoneal cavity in all cases of peri- . . . toneal soiling. In spite of the encouraging reports from other clinics, we have not seen any appreciable decrease in the number of cases of peritonitis since we began the use of sulfanilamide intraperitoneally. In twenty-seven cases in which sulfanilamide powder was placed in the peritoneal cavity and sulfona- . . . mides were used systemically after operation, eight patients lived and nineteen died, which gives a mortality of 70.4 per cent. Therefore, in our hands, at least, the use of sulfonamides has not appreciably lowered the mortality. In spite of the poor showing made by the use of sulfonamides in our hands, it does



TABLE XV. THORACIC-ABDOMINAL WOUNDS: TWELVE FATAL CASES

CASE NO.	SEX AGE	ENTRANCE WOUNDS OF ABDOMEN	ENTRANCE WOUNDS OF CHEST	OPERATIVE FINDINGS	PNEUMO-THORAX	TIME D
1	M 16	Right lower quadrant	4th right interspace anterior axillary line; subcutaneous emphysema	--	--	45 min admission opera
2	M 35	Right lower quadrant; right costal margin in right upper quadrant	4th right intercostal space	--	--	30 min admission opera
3	M 35	Right lower quadrant	4th interspace mid clavicular line (right arm middle upper third)	--	--	10 min admission opera
4	M 15	--	2nd right interspace anterior axillary line (lateral aspect right arm)	Perforation of right diaphragm, dome of right liver, left kidney	Minus 3, plus 4, right side	3rd positive
5	M 27	--	--	Perforation of stomach and diaphragm	--	1st positive
6	M 29	--	--	Perforation of right lobe of liver and diaphragm	Underwater drainage	1st positive
7	M 21	--	Left intercostal space anterior axillary line; subcutaneous emphysema	2 penetrations of right lobe of stomach	Tension pneumothorax; underwater drainage	2 hr. admission opera
8	M 35	--	7th left intercostal space anterior axillary line; subcutaneous emphysema	Perforation of diaphragm and stomach	Underwater drainage	1st positive
9	F 23	--	3rd right intercostal space midclavicular line (gunshot wound in right temporal region of skull)	4 perforations of jejunum and 2 of stomach	--	1st positive
10	M 47	--	Left side of chest at level of 6th dorsal vertebra (neck, left supraclavicular region)	2 perforations of jejunum	--	40th positive
11	F 30	Left upper quadrant; right upper quadrant	Left postaxillary line level of 8th rib	4 perforations of jejunum and 2 of stomach	--	1st positive
12	M 22	--	Jagged bullet wound beneath angle of right scapula at level of 7th dorsal vertebra	8 perforations of small intestine, 2 of stomach, 1 of gall bladder	--	1st positive
13	M 19	--	Anterior axillary line near nipple	Laceration of spleen and dome of diaphragm	--	2nd positive
14	M 65	--	3 penetrating wounds of chest at right anterior axillary line at level of 8th rib, exit at 2nd rib; another bullet wound at level of 3rd right intercostal space	Laceration of liver and perforation of diaphragm	Plus 10, plus 2; underwater drainage	1st positive

not mean that we do not favor their use, because we feel that in a larger number of cases they will help prevent peritonitis. On the other hand, the use of sulfonamides certainly cannot, and never will, take the place of good surgery.

We have used penicillin in five cases in this series, but it is too early for us to draw any conclusions from its use. We do feel that it will help in certain cases and we advise its use postoperatively.

Perforations of hollow viscera were usually repaired by means of purse-string sutures or interrupted Lembert sutures. Injuries to the liver were packed or sutured if there was active bleeding. Injuries to blood vessels were treated by ligating the bleeding vessel. Injuries to the spleen were treated by splenectomy. In this group of cases, operations, other than suturing of perforations of the gastrointestinal tract and diaphragm, were performed as shown in Table XVI.

TABLE XVI. OPERATIONS OTHER THAN

AND DIAPHRAGM

OPERATION	NUMBER OF CASES
Splenectomy	6
Exteriorized intestine	3
Suprapubic cystostomy	3
Resection of small intestine with side-to-side anastomosis	3
Nephrectomy	1
Removal of coccyx and lower part of sacrum	1
Cecostomy	1
Resection of small intestine with anastomosis over a Murphy button	1
Cholecystectomy	1

There were three patients with laceration of the spleen in which splenectomy was done and all three died. In the series the intestines were exteriorized—the small intestine in one. The patient with the large intestine exteriorized had four through-and-through perforations of the transverse colon and died on the third postoperative day. In the cases of perforation of the small intestine in which the intestines were exteriorized, one patient lived and one died, they both had multiple through-and-through perforations of the small intestine. The three patients on whom a suprapubic cystostomy operation was performed lived. In three cases resection of the small intestine was done because of multiple through-and-through perforations and these three patients died. In one case a Murphy button was used for anastomosis and the patient died. It has been our experience that resection of the small intestine is a procedure fraught with a high mortality. Suture of the individual perforations is the procedure of choice and we have never seen intestinal obstruction occur as a result of suture of multiple perforations of the intestines. Obviously, if a large blood vessel of the mesentery is injured, the surgeon has no choice and should resect the affected segment of bowel. Under such circumstances, the Murphy button should be used because of the rapidity with which the anastomosis can be made.

In one patient with laceration of the kidney, a nephrectomy was performed and the patient died on the twelfth postoperative day.

Postoperatively all patients should receive blood transfusions and intravenous fluids to combat postoperative shock, correct electrolyte imbalance, and overcome dehydration. The use of sulfonamides and penicillin is recommended in all cases where there has been perforation of a viscus, excepting the spleen.

In most cases in this series drainage was carried out when there was spillage in the peritoneal cavity. Our staff is still divided as to the advantage and necessity of drainage. It is our feeling that a small Penrose drain does no harm and does not add to the mortality, but, in fact, may prevent an occasional death from peritonitis. Drainage does not, however, take the place of careful toilet of the peritoneal cavity at the time of operation or of gentle handling of tissues commensurate with the necessary speed that is indicated in these operations.

#### SUMMARY

Despite the increasing number of excellent clinical reports of large groups of cases, we have attempted to emphasize certain facts which we felt needed to be constantly brought to the attention of surgeons who are engaged in this work.

1. The presence of abdominal rigidity and tenderness is the most valuable clinical sign of penetrating wounds of the abdomen.

2. A positive abdominal tap or the finding of a pneumoperitoneum on radiographic examination is a valuable diagnostic sign of abdominal penetration in some cases.

3. Immediate operation is indicated in all penetrating wounds of the abdomen; shock is no contraindication. The surgeon should be alert to reduce to a minimum the time between the admission of the patient to the hospital and operation.

4. Blood transfusions and intravenous fluids should be used to reduce shock and effect the necessary fluid balance; this is an immediate and urgent part of the treatment on admission.

5. The surgeon should use sufficiently large incisions to give adequate exposure because a substantially large reducible factor in mortality is caused by missed lesions.

6. Sulfonamides do not take the place of good surgery, but they should be used because we consider them potentially valuable adjuvants. Penicillin should be used postoperatively in cases where there has been a perforation of the gastrointestinal tract.

7. Extreme shock is often indicative of blood vessel injury. Early death upon arrival in the hospital is usually due to an injury of a large blood vessel.

8. "Liver deaths" explain some deaths where there is liver injury that is not primarily due to shock and hemorrhage.

9. Too few papers on this subject detail the post-mortem findings in the fatal cases.

10. Age and physical condition of the patient at the time of injury and the presence or absence of associated injuries are definite factors affecting mortality.

In conclusion, there is no group of wounds which requires more early, energetic teamwork and cooperation on the part of the entire hospital staff and nursing service than gunshot wounds of the abdomen, and a recognition of this fact will be an appreciable factor in the reduction of mortality from such injuries.

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# ACUTE PULMONARY EDEMA ASSOCIATED WITH MEDIASTINAL EMPHYSEMA

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**M**EDIASTINAL emphysema has become recognized as a rather common condition with important clinical aspects. The methods of production are now well understood as a result of experimental studies. Emphysema of the mediastinum has been observed in the following circumstances: as a pre-operative and postoperative complication of tracheotomies;<sup>1-4</sup> as a result of blunt trauma to the chest wall, frequently associated with, but not due to, fractured ribs;<sup>5</sup> as a spontaneous occurrence;<sup>6-12</sup> during parturition;<sup>14</sup> during an acute asthmatic attack;<sup>15</sup> as a complication of penetrating wounds of the trachea or bronchus; as a complication of intratracheal anesthesia;<sup>16</sup> after the induction of artificial pneumothorax;<sup>7</sup> as a complication of foreign bodies in the bronchi;<sup>13</sup> and in the presence of unrelieved respiratory obstruction.<sup>2, 13</sup>

## CAUSES OF MEDIASTINAL EMPHYSEMA

The experimental work of Macklin and Fischer<sup>13, 17, 18</sup> has done much to clarify the pathogenesis. As a result of overinflation of the pulmonary alveoli, air ruptures into the interstitial tissue of the lung and dissects within the sheaths of the pulmonary vessels to the mediastinum. This is the mechanism of production in those conditions which produce increased intra-alveolar pressure. Thus, it is the mechanism in laryngeal obstruction, foreign bodies in the bronchi with extrusion efforts, during an asthmatic attack, during expulsion efforts in labor, as a result of overinflation during intratracheal anesthesia, in the spontaneous variety, and as a result of blunt trauma to the chest wall.

Some cases of spontaneous mediastinal emphysema develop immediately after severe coughing. Others occur in newborn infants who may have some degree of respiratory obstruction or a compensatory dilatation of the alveoli because of an ateleclasis. However, in some cases no cause of alveolar rupture is discernible.<sup>6-12</sup> An aid in the diagnosis of mediastinal emphysema is the presence of loud crepitant râles heard over the precordium which are synchronous with each heartbeat. Hamman<sup>6</sup> described it as a "peculiar crunching, crackling, bubbling sound heard over the heart with each contraction." The sound is sometimes heard only with the patient in certain positions. The presence of subcutaneous crepitation confirms the diagnosis.

Mediastinal emphysema occurring after induction of artificial pneumothorax is probably due to injection of air into the interstitial tissue of the lung through a pleural adhesion.<sup>6</sup>

A common method of production of mediastinal emphysema, which may not involve pulmonary overflation, occurs during tracheotomies performed to

relieve obstruction of the upper respiratory passages. After the deep facial planes of the neck have been entered and before the trachea has been opened, the extreme inspiratory efforts suck air into the mediastinum from the exterior through the operative incision.

The third mechanism of production is less common. Traumatic perforations of the trachea or bronchus may permit the escape of air into the deep fascial planes and produce a massive mediastinal emphysema.

#### EFFECTS OF MEDIASTINAL EMPHYSEMA

It is now well established that when sufficient intramediastinal tension develops, air ruptures through the mediastinal pleura into the pleural cavity, producing a pneumothorax.<sup>19</sup> A review of the cases in Roper Hospital in a five-year period reveals three such instances. Numerous cases have been reported.<sup>3, 4, 18</sup> Neffson<sup>1</sup> found seventeen instances in 126 tracheotomies. Injury to the pleura during a tracheotomy frequently has been blamed, but the reported cases reviewed at autopsy have revealed that the pleural domes were intact, indicating that the intrapleural air extended from the mediastinum.

A serious complication of mediastinal emphysema is interference with the circulation in the pulmonary vessels and the consequent development of acute pulmonary edema. Air under pressure in the mediastinum surrounds and obstructs the vessels, obstruction of the pulmonary veins occurring before obstruction of the pulmonary arteries. More blood is forced into the lung than can escape, and the pressure within the pulmonary capillaries rapidly rises. Transudation of fluid from the capillaries occurs and acute pulmonary edema results. The possibility of circulatory failure has been mentioned in the literature<sup>8, 18, 19</sup> but no clear-cut cases of acute pulmonary edema have been reported.

#### CASE REPORT

A 28-year-old Negro man was admitted to Roper Hospital (Case 26186) Jan. 30, 1944, about forty-five minutes after receiving a stab wound of the neck, inflicted by a "switch-blade" knife. Physical examination revealed a well-developed, dyspneic, apprehensive Negro man, complaining of substernal pain and in obviously acute distress. Blood pressure was 120/70, pulse rapid but of good volume. There was a penetrating wound of the neck, about 1 cm. in length, situated just to the left of the midline at the level of the first or second tracheal ring. Both air and blood bubbled back and forth through the wound with each respiration and it was obvious that the trachea had been penetrated by the knife. The neck was distended and palpation revealed the characteristic crepitation of subcutaneous emphysema. Further palpation demonstrated subcutaneous air in the region of both shoulders, the face, upper eyelids, forehead, and superior portion of the thorax. Because of the interference with auscultation by the loud crepitation over the chest, interpretation of the physical signs of the cardiopulmonary examination was difficult; it was thought, however, that left hemopneumothorax was present and that some pneumothorax had occurred on the right side. Radiographic examination of the chest revealed evidence of extensive emphysema of the mediastinum and the soft tissues of the neck, back, shoulders, and lateral chest walls. The remainder of the examination was noncontributory.

Shortly after admission, the administration of oxygen by nasal catheter was begun. It was noted that the emphysema was spreading rapidly. Coincidentally, the patient became more dyspneic and his blood pressure was falling. Accordingly, one hour after admission, a tracheotomy was done at the level of the second tracheal ring under local anesthesia. On

return from the operating room, the patient was breathing more easily but the pulse was rapid and weak and the blood pressure was 100/60. Continued fall in blood pressure was interpreted as shock and, consequently, 500 c.c. of plasma with 500 c.c. of normal saline solution were administered intravenously. Almost immediately after completion of the intravenous infusion, the patient's respiration became labored and irregular and, in spite of continuous oxygen and cardiorespiratory stimulation by metrazol, coramine, and caffeine, he died three hours after operation.

Examination of the body at autopsy revealed that the trachea had been penetrated through both its anterior and posterior walls. Subcutaneous and mediastinal emphysema was pronounced, the latter extending from the root of the neck to the diaphragm. Each pleural cavity contained a small amount of air and about 450 c.c. of clear straw-colored fluid; no blood was noted. Both lungs were boggy and permitted the escape of much frothy material on pressure. Careful examination failed to reveal any evidence of perforation of the apical pleura on either side. There were no other findings of significance. The necropsy diagnosis was penetrating wound of trachea, bilateral hydropneumothorax, subcutaneous emphysema, and acute pulmonary edema.

*Comment.*—This case represents an example of acute pulmonary edema produced by compression of the pulmonary veins in the mediastinum incident to the massive accumulation of air. It is noted that death occurred after the further production of mediastinal emphysema had been halted by the tracheotomy. The fatal outcome was certainly influenced by the administration of intravenous fluids which raised the pressure in the already overloaded pulmonary capillaries. In retrospect, withdrawal of several hundred cubic centimeters of blood would have been more rational than the intravenous administration of plasma and saline solution.

A small amount of air was found in each pleural cavity at autopsy. Careful dissection of the pleural domes failed to reveal any evidence of injury, indicating that air progressed from the mediastinum to the pleural cavity to produce the pneumothorax. The volume of pneumothorax was small, however, and probably did not greatly influence the course.

#### CLINICAL IMPLICATIONS

Numerous points of clinical significance may be derived from a review of the causes and effects of mediastinal emphysema. Conditions producing markedly increased intra-alveolar pressure should be avoided or relieved as soon as possible. The often heard plea for early tracheotomies when laryngeal obstruction is progressing is re-emphasized. Preliminary insertion of a bronchoscope into the trachea is indicated in many cases of inflammatory laryngeal obstruction. The tracheotomy may then be done with the bronchoscope in place as an airway. Free communication with additional fascial planes of the neck by dissecting away the investing fascia of the trachea during the tracheotomy should be avoided. The trachea should be opened as soon as possible after the deep fascial planes are entered, in a patient who has laryngeal obstruction.

Intravenous fluids should be omitted in the presence of unrelieved respiratory obstruction, and in any patient who has mediastinal emphysema. If the latter condition produces a dangerous degree of tension, it should be decompressed by a low transverse cervical incision, the mediastinum then being entered by blunt dissection.<sup>5</sup>

A careful examination for pneumothorax should be carried out in all situations in which mediastinal emphysema occurs, particularly after tracheotomies for laryngeal obstruction. Air should be aspirated if it is producing respiratory embarrassment. If tension pneumothorax develops, provision must be made for the continuous escape of air from the pleural cavity by closed decompression.

#### SUMMARY

The cause and effects of mediastinal emphysema are reviewed. An additional effect, acute pulmonary edema, is discussed and a case presented.

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# Editorial

## Venous Interruption in Thrombo-Embolic Disease

**I**NTERRUPTION of the femoral veins at the groin, since it was first described by Homans in 1934, has become an accepted method to prevent fatal pulmonary embolism. Unfortunately, but not unexpectedly, as with any new method of treatment, serious complications from the operation are being reported in the literature. The chief one is that instances of interference with the circulation of the extremity occur following the operation. A analysis of these reveals that too much of the venous return from the leg had been interrupted. In some cases not only the common femoral vein but also the saphenous had been interrupted and in some instances a block resection had been one of the femoral vein including the saphenofemoral junction and the proximal ends of the superficial and deep femoral veins. In view of these cases it seems worth while to draw attention to the fact that femoral vein interruptions have been carried out in over 1,000 patients at the Massachusetts General Hospital without a single instance of serious interference with the circulation of the extremity, and the mortality rate from the procedure has been zero. It is felt that this is because we adhere to certain basic principles, and in order to help prevent further catastrophes it seems worth while to innumerate them.

The chief indications for bilateral femoral vein interruption are (1) the presence of venous thrombosis in the deep veins of the lower extremity, (2) the occurrence of a nonfatal pulmonary embolus irrespective of whether or not the legs show signs of venous thrombosis, (3) a concomitant rise in temperature, pulse, and respiration postoperatively in a patient that cannot be explained by some other cause, (4) venous thrombosis diagnosed in one extremity, even though no signs of venous thrombosis are detected in the other, and (5) as a prophylactic measure in patients over 50 years of age who are subjected to major abdominal or pelvic operations for malignant disease. This may be performed as a separate operation or at the same time as the major operative procedure. Prophylactic interruption has also been carried out with good results in elderly patients with fractures of the hip. It is especially valuable in patients with an intratrochanteric type of fracture because of the high incidence of fatal pulmonary embolism in this group.

The purpose of the operation is to interrupt the long column of blood in the femoral and popliteal veins, so that if a clot forms in them it cannot be swept upward to lodge in the pulmonary artery. Interruption of the superficial femoral vein just distal to its junction with the deep femoral may be carried out without danger to the circulation of the extremity in any patient irrespective of his age. It is the safest level for the average surgeon to interrupt this large venous system, since the vessel at this point is free of any tributaries. At the

same time the long venous channel of the legs is interrupted at a sufficiently high level to prevent fatal embolism. The vein may be tied in continuity, but division of it and ligation of each end with a primary ligature and a secondary stitch ligature distal to it in each stump is considered the better procedure. These ligatures should be of the nonabsorbable type, either silk or cotton. The safest method of anesthesia in the postoperative or very ill patient is local infiltration of 1 per cent procaine solution.

Minor pulmonary emboli following femoral vein interruption have occurred in about 5 per cent of our cases. The majority of these probably arise from the profunda femoris branch or the common femoral vein above the point of interruption. Only two deaths from pulmonary embolism have occurred following bilateral femoral vein interruption in our series of 1,000 patients. The superficial femoral veins had been interrupted in one and the common femorals in the other. Neither patient died of a sudden massive embolus, but succumbed to the cumulative effects of relatively small emboli arising from clots in the iliac veins which were superimposed on the ones occurring prior to the vein interruptions.

In some cases, to prevent these postinterruption emboli it is considered a better operation to interrupt the common femoral vein proximal to the profunda branch. In general, this type of interruption should be reserved for those patients in whom a thrombus is found in the common femoral vein, since a secondary thrombus is more apt to form after removal of the primary one than if none was present, and later be dislodged by back pressure in the profunda femoris vein. The surgical interruption of the common femoral vein, if it contains a thrombus, will not endanger the circulation of the extremity, since it already has been occluded. The common femoral vein is relatively short and several large tributaries drain into it, so that it is a more difficult procedure to interrupt it than the superficial femoral vein. One or two of these branches usually must be ligated and divided separately to give sufficient length of vein to permit its safe division and ligation. The division should be distal to the saphenofemoral junction, leaving the saphenous vein as a collateral channel for the venous return. Under no circumstances should the common femoral and the saphenous vein both be interrupted, unless it is found that they are already occluded with thrombi. This is especially true in elderly patients with deficient arterial circulation, since apparently they have as poor a venous collateral as they do an arterial one. A good rule is that unless the dorsalis pedis and posterior tibial arteries can be palpated in the feet, the superficial femoral vein should be interrupted and not the common femoral, unless the latter is already occluded by a thrombus.

Pain and swelling of the leg secondary to thrombophlebitis do not always subside following femoral vein interruption and in a few instances they become more marked due to a spread of the thrombosis distal to the site of vein interruption. In these patients, as an adjunct in treatment, marked amelioration of the pain and swelling can be obtained by paravertebral procaine injection of the lumbar sympathetic chain, as has been recommended by Ochsner.

Interruption of the venous system at a higher level, namely, the inferior vena cava or the common iliac veins, should not be done routinely but reserved

for the unusual case of thrombo-embolic disease, in which the femoral veins have been thrombosed for one week or more and pulmonary emboli are still occurring. This is because the thrombi at this stage of the disease are so adherent that it is impossible to remove them through the femoral veins. Inferior vena cava interruption is also indicated in patients who are having septic pulmonary emboli from sepsis in the pelvis or lower extremities. This is preferable to bilateral common iliac vein interruptions, because the venous systems from both extremities can be interrupted through a single exposure. It should be remembered that it is a major surgical procedure requiring general or spinal anesthesia in contradistinction to femoral vein interruption. The development of postphlebitic lower leg ulcerations and varices of the abdominal wall following inferior vena cava interruption are additional reasons that the operation should not be used routinely in the treatment of thrombo-embolic disease. In a group of twelve caval interruptions in the clinic at Massachusetts General Hospital, two patients have developed indolent ulcers of the lower leg and a third patient has had bilateral recurrence of them, whereas only one transient postphlebitic ulcer has occurred in the group of 1,000 patients with femoral vein interruption.

It is our opinion that if these general principles of venous interruption in the treatment of thrombo-embolic disease are followed, lives will be saved from fatal pulmonary embolism and serious complications will be eliminated. Furthermore, this procedure eliminates the long convalescence necessary in the conservative treatment of thrombophlebitis.

Finally, it should be pointed out that the interruption of these large veins should not be entered into too lightly by the average surgeon unaccustomed to dealing with large blood vessels. Alarming hemorrhage may occur if the femoral vein or one of its tributaries is accidentally torn and the femoral artery may be irreparably damaged in attempting to control it.

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# SURGERY

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## Original Communications

### PRINCIPLES IN REPARATIVE PLASTIC SURGERY

#### EXPERIENCES IN A GENERAL HOSPITAL IN THE TROPICS

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**P**ROBLEMS in plastic surgery in a general hospital in the communications zone predominantly are those of closure of war wounds. Observations and principles reported here are derived from experiences with 4,040 surgical battle casualties from the Philippine campaign. These were admitted during the period of Oct. 25, 1944, to March 25, 1945. A less important source of admission was provided by burns, trauma, and the ever-prevalent tropical ulcer incident to the activities of personnel in the tropics.

Transportation problems in the vast Pacific distances exerted a profound influence upon the choice of surgical procedure. Forty-nine per cent of casualties admitted during the first six weeks during the battle for Leyte came under our care five to eight days after injury. During the Luzon campaign, 36 per cent of 1,566 patients had been under care in evacuation hospitals or on ship en route for twenty-one to fifty-five days. Thus, this surgical service was confronted with an ever-changing picture of wound condition. The aim to evacuate no patient to the United States with unhealed wounds was based on the knowledge that patients would receive nothing other than emergency surgical care during the five-week period after they were removed from our wards. The attainment of this goal was prevented by the need for hospital beds during a brief period and by the physical limitations of the operating staff.

Embodied in this report are 468 secondary closures, 306 split-skin grafts, 46 small deep grafts, and 28 primary procedures involving the transplantation of flaps of skin and subcutaneous tissue. Recent wounds are more suitable for secondary closure. There is a definite loss of elasticity of the skin and subcutaneous tissue in older wounds even though there is no loss of tissue. Despite wide undermining, the margins of older wounds cannot be approximated without dangerous tension. Hence, skin grafting was employed more frequently in the care of older wounds. We have seen little indication for flap or tube grafting. This is a mission of the reconstructive centers in the United States.

The nature and the scope of intermediate or reparative surgery have been clearly stated by Churchill in relation to the European Theater of Operations. The prompt closure of wounds prevents infection and contracture, converts compound into simple fractures, and prepares for early reconstructive surgery. In the Pacific Theater of War, the chain of evacuation is so prolonged that the hazard of nitrogen loss from wound secretions is an additional factor demanding consideration. The efforts of reparative plastic surgery in a general hospital in the Pacific Theater are directed, first, to an appraisal of the wound and selection of a course of preoperative wound therapy; second, to the selection of the appropriate operative procedure; and finally, to the performance of the operation and attention to postoperative care. We believe in the paramount importance of the preoperative care of the wound and the necessity for sound surgical judgment in choosing the time and mechanics of the operation. To this effect, it was possible to train eighteen medical officers without previous experience in skin grafting or secondary wound closure. Rapidly they developed operative skill and knowledge of postoperative care so that they could perform split grafting effectively. But these medical officers could not be developed in their surgical judgment in wound care or in selection of operative procedure during the brief period while they were under training.

#### OBSERVATIONS ON WOUNDS

*Condition on Admission.*—This series of battle casualties permitted observation of large numbers of wounds at increasing intervals of time following initial surgery in the forward echelons. These intervals ranged from five to sixty days. Wounds which had been treated by frequent change of dressings were in much better condition than those treated by the closed method. Treatment during this interim was limited to supportive measures and chemotherapy. Packing of wounds with petrolatum gauze for transportation of the patient now is popularly condemned. Wounds so treated frequently showed extensive infection at the time of admission. Reparative surgery performed during transport on hospital ships failed in a high percentage of cases.

Cultures of wounds taken at the initial dressing commonly showed mixed infection. *Bacillus proteus*, *Bacillus pyocyaneus*, and staphylococcus were the common contaminants of wounds. Beta hemolytic streptococci were found rarely. Diphtheroids were recovered on culture frequently. *Clostridium welchii* was found in thirty-seven cases of clinical gas infections or gangrene and as a surface contaminant of 138 other wounds in the series of 4,040 battle casualties.

Observation of these wounds of varied type suggested a simple classification which was used as the basis for selection of operative procedures. The wounds were grouped as follows:

1. Recent clean wounds without invasive infection and ready for reparative surgery after brief treatment (Fig. 1, A and B).
2. Recent wounds which are infected and complicated by devitalized tissue or retained foreign body and in need of further débridement or extension of drainage (Fig. 2, A, B, and C).



A.

B.

Fig. 1—  
result of han  
retention.

... recent wound of soft tissue ready for grafting. B, Result of débridement and frequent change of wet dressings of azochloramide 1:3300 solution; ready for grafting. C, Result of application of hand-cut split-thickness grafts, no sutures used. Grafts retained with mesh gauze and collodion. Immobilization in plaster hip spica. Saline dressings changed through window in cast. Several small blebs can be seen on the surface of the graft; these were caused by tiny wood fibers extruded to the surface.



A.

B.

C.

Fig. 2.—A, Three stages in the treatment of a recent wound complicated by devitalized tissue and retained foreign bodies; appearance on admission. Wound caused by explosion of a Japanese shell. B, After débridement and frequent change of wet dressings of azochloramide 1:3300 solution; ready for grafting. C, Result of application of hand-cut split-thickness grafts, no sutures used. Grafts retained with mesh gauze and collodion. Immobilization in plaster hip spica. Saline dressings changed through window in cast. Several small blebs can be seen on the surface of the graft; these were caused by tiny wood fibers extruded to the surface.

- 3 Late clean granulating wounds, including those with advanced scarring and contracture (Fig. 3, *A* and *B*).
4. Late chronically infected wounds with exposed bone (Fig. 4), tendon (Fig. 5), or other complications such as pyoarthrosis, osteomyelitis (Fig. 6) or anaerobic infection (Fig. 7).

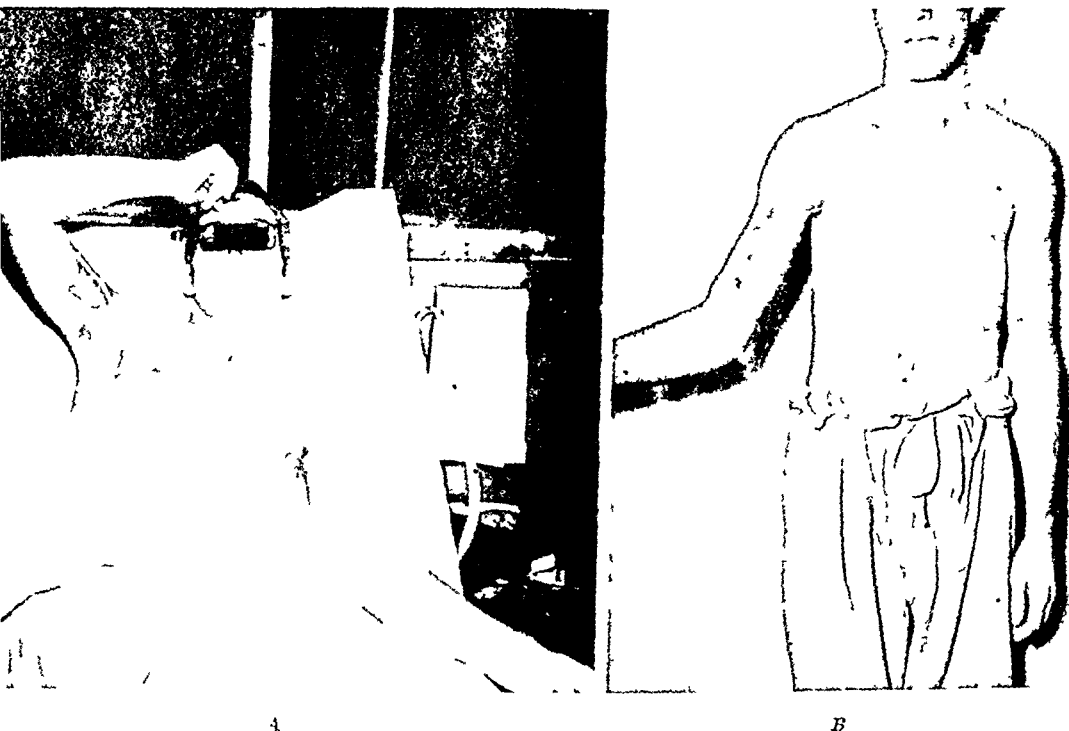


Fig 3—*A*, Appearance at the time of admission thirty-two days after débridement for bullet wound. This is an example of a late clean granulating wound with advanced scarring and contracture. The margins of the wound are indurated and tense for a distance of 5 cm. The elbow cannot be extended beyond an angle of 90 degrees. *B*, Sixteen days after the application of a split-thickness graft to granulating surface. Contracture limits extension but edema and induration are subsiding. The patient is receiving physiotherapy and the extension has improved.

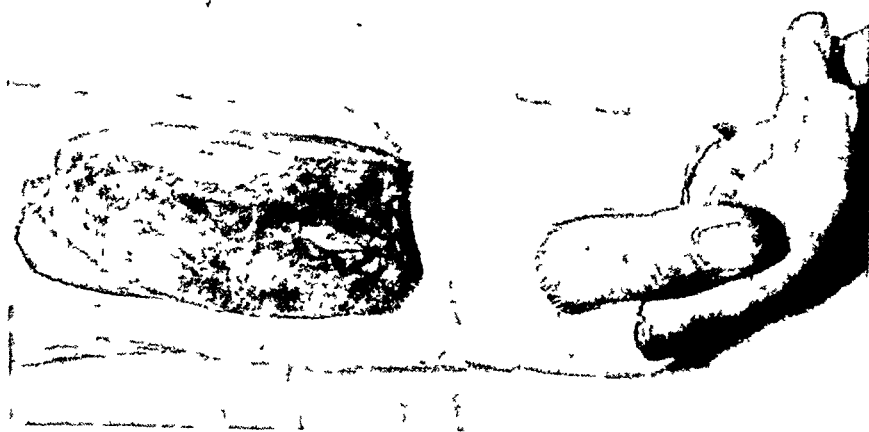


Fig 4—An example of a late chronically infected wound with exposed bone

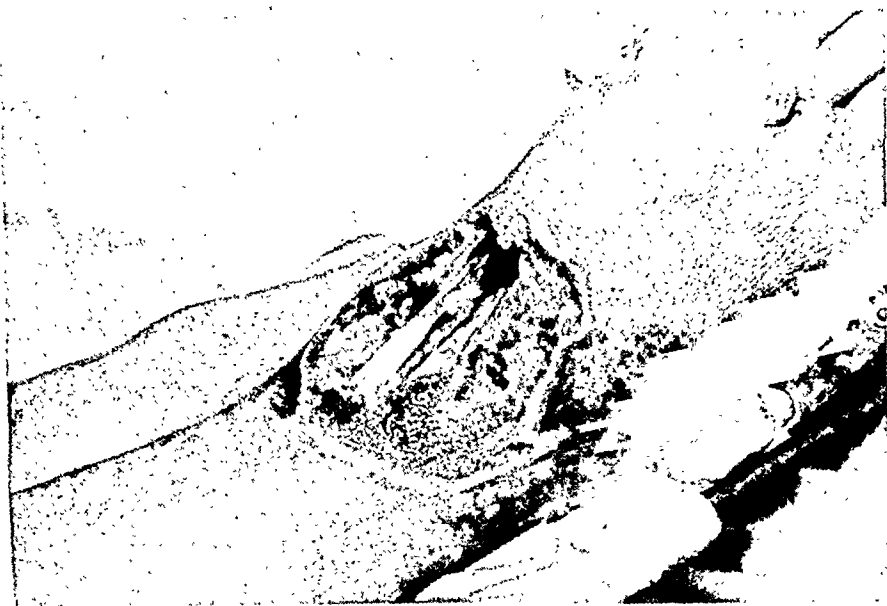
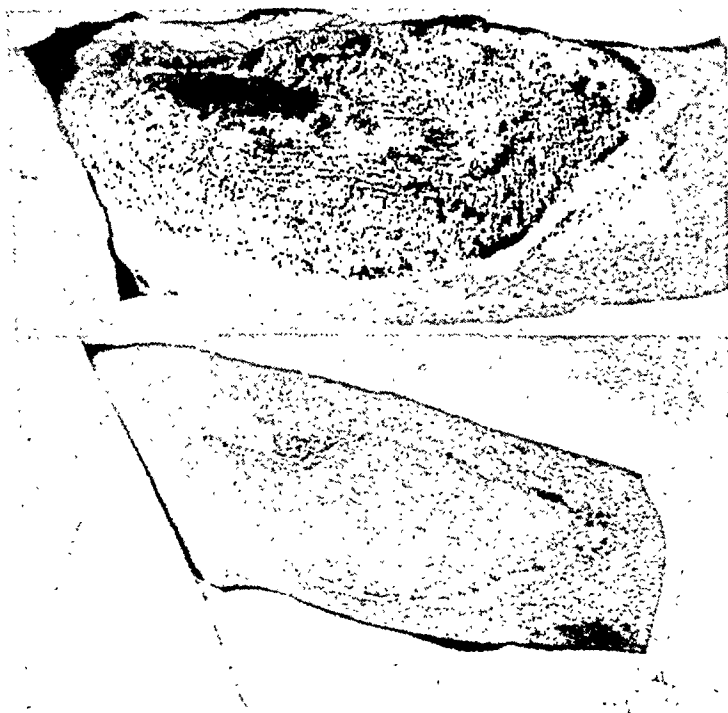


Fig. 5.—An example of a late chronically infected wound with exposed tendon.

A.



B.

Fig. 6.—A, Large chronically infected wound with massive defect of the interior thigh associated with compound fracture and osteomyelitis of the femur. Wound caused by a Japanese dum-dum bullet which entered the posteromedial aspect of the thigh. A pus-filled sinus at the upper left drains from the fracture site. B, Result twenty-two days after the application of a dermatome graft. The sinus still drains pus. A rent at the margin of the graft for drainage remains unhealed. Ward procedure: skeletal traction undisturbed, open dressing technique. A few necessary sutures were used to overcome the contraction of the graft induced by the rubber cement. In this case the graft affords a permanent cutaneous surface.



5. Early and late second and third degree infected burns (including phosphorus burns).

*Preoperative Treatment.*—Physiologic reactions to tropical environment must be considered when planning any regimen of preoperative wound care.

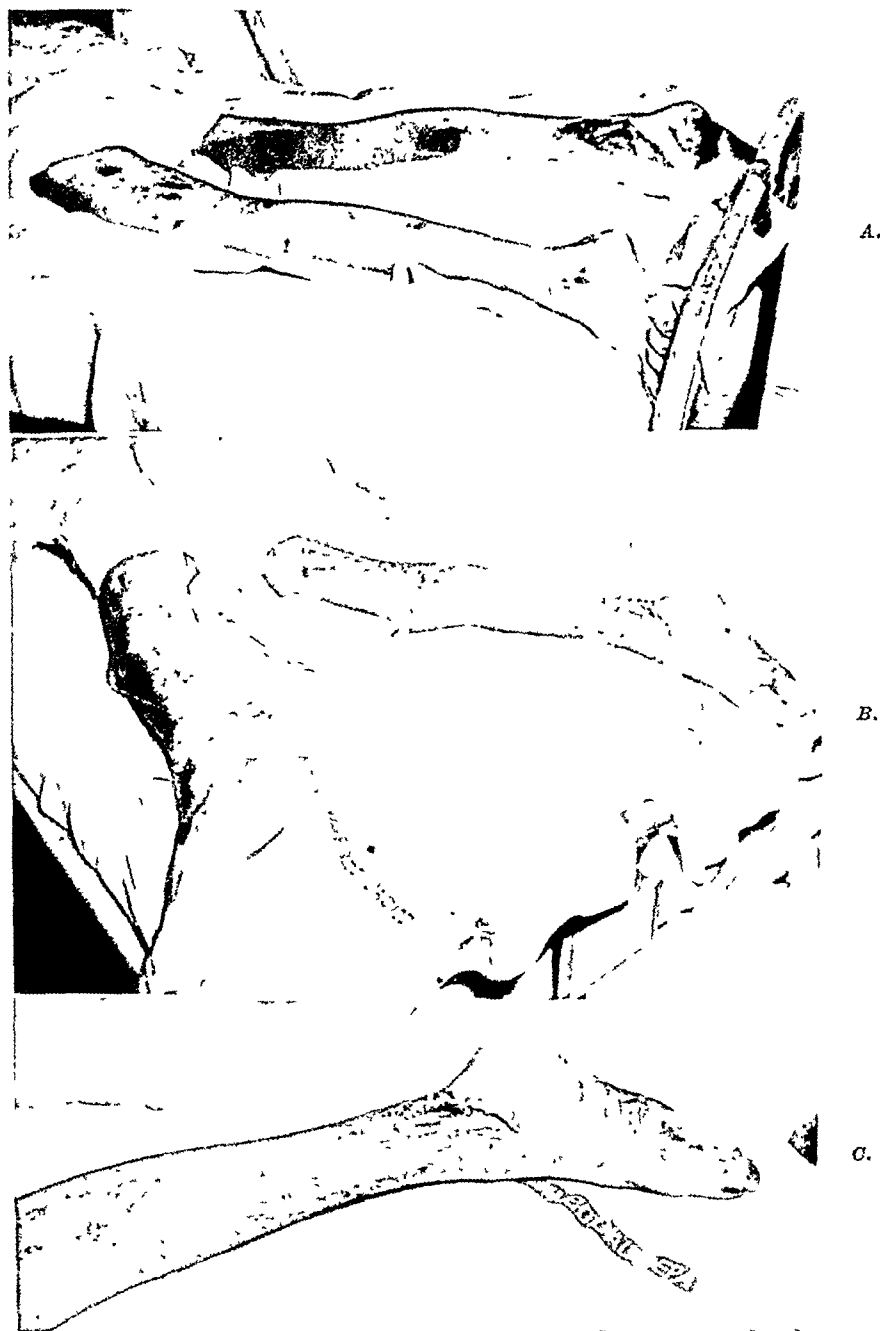


FIG. 7.—A, Late chronically infected wound with exposed Achilles tendon secondary to débridement for gas gangrene. Injury by Japanese mortar fire. B, Sixteen days after application of split grafts. C, Detail view of the leg and foot. Note that the graft which was wrapped around the tendon has taken completely.

The cornified layer of the epidermis is thin and deficient in the tropics. Deeper layers of cells are hydropic and immature. There is more intense proliferative activity in the stratum germinativum and constant sweating leads to maceration and rapid desquamation of the poorly keratinized layers. Unless constantly removed, this moist epithelial detritus is a culture medium for *B. pyocyaneus*, *proteus*, diphtheroids, and staphylococci and provides a source of constant recontamination of the wound. Folliculitis and impetigo are found often under occlusive dressings, particularly if they are greasy. Dermatologists learned early in their experiences in the tropics that skin will not tolerate petroleum products.

In the preoperative care of wounds, wet dressings of 1:3300 aqueous solution of azochloramid were employed. These were changed at four-hour intervals. The initial step in wound care was the removal of any necrotic tissue by sharp dissection. Many wounds were ready for closure or graft in twenty-four to forty-eight hours following the institution of such treatment upon arrival at a general hospital. Attention to the wound margins and the surrounding skin is an essential feature of dressing care for the reason indicated previously. Persistent drainage from a sinus was indication for search for buried foreign body. Saline dressings were used on those few patients who showed irritation of the skin from azochloramid. A mild astringent in the form of dilute potassium permanganate solution was found to be useful in controlling surrounding dermatitis. The local application of penicillin to wounds was found to be a useless extravagance. Compresses moistened with penicillin were effective only when changed frequently. The same result could be obtained with saline dressings. One hundred thirty-eight wounds were treated with penicillin packs. Dressings were changed at twenty-four-hour intervals. Ten cubic centimeters of penicillin solution (250 units per cubic centimeter) were added to the pack at six hourly intervals. There followed such a striking increase in wound exudate and in the growth of gram-negative organisms that this type of treatment was promptly abandoned. This same treatment was used later on the occasional wound infected with beta-hemolytic streptococci. Improvement was prompt and sustained in such instances. Sulfonamide drugs were not used locally in the treatment of wounds. Systemic administration of sulfadiazine or penicillin was limited to patients who were febrile or toxic, or whose wounds showed streptococci or evidence of spreading infection. Patients were not operated upon until the red blood cell count and plasma protein content of the blood had been restored to normal values by the transfusion of whole blood or plasma.

*Choice of Operative Procedure.*—Secondary suture unquestionably is the best method of closing war wounds whenever practicable. It provides full skin and subcutaneous tissue covering for the defect and in our experience allows for the excision of much of the newly formed scar tissue which causes deformity. However, our ratio of 4.6 closures to 3.0 grafts does not seem to support this contention. The more obvious factors leading to the selection of a grafting procedure are loss of substance and wound complications such as exposed bone or tendon, persistent drainage from a fracture site, or infection of joints. Cer-

tain anatomic locations are not suitable for secondary closure. Another factor of importance in our experience was the age of the wound. Unhealed wounds over four weeks old are less suitable for closure. In such wounds the skin has retracted and is indurated for a considerable distance from the wound margin. An occasional problem is presented by a wound of an extremity which is considerably swollen. Closure in such a case cannot be effected without undue tension. Usually this condition will persist until the wound is healed. In such a case skin grafting is preferable to secondary closure. The resolution of inflammatory products begins promptly after healing. In all probability a fair percentage of the grafts in this type of case should be excised in the reconstructive centers. At a later date the grafts may be excised and the defect closed with an assurance of success that did not exist when the patients were undergoing reparative surgery. Others will need replacement with pedicled flaps. Thus, in reparative war surgery, the thick-split graft may serve as a temporary surface. It was found that it was important to avoid secondary closures in the region of the elbow, distal third of the forearm, and the hand. Similarly, closure of wounds of the groin, knee, distal third of leg, ankle, and foot are less likely to succeed. In other regions there has been no hesitation in undermining to any extent necessary, in adding secondary incisions, or in swinging flaps from neighboring areas in order to effect coaptation without tension.

#### SECONDARY CLOSURES

Secondary closure was performed in 468 patients during the five-month period. It was possible to keep careful record of only the first 211 of these operations. The average duration of time from injury to closure in this group was twenty-four days. This was due to the transportation problems and the fact that the influx of patients was so rapid that an actual bottleneck existed in the available operating rooms. Complete healing was obtained in 181, or 85.7 per cent. Partial wound separation occurred in 16, or 7.6 per cent; complete failure in 14, or 6.7 per cent. The relatively long period between injury and secondary closure led us to adopt excision of the wound as a preliminary to suture. Scarred wound margins, granulation tissue, and scar were excised en bloc to the level of the deep fascia. Fine catgut was used for hemostasis. After adequate mobilization of the skin and subcutaneous tissue, the wounds were loosely closed with vertical mattress sutures catching the floor of the wound. These sutures were sometimes tied over bolsters to prevent cutting. Counter-drainage at the margin of a large undermined area was employed occasionally. Precise suturing in an attempt to obtain cosmetic results is not advised. Oozing may continue from the scarred floor of the wound. Serum collection is usual. A loosely closed wound treated with wet dressings will evacuate blood and serum between the sutures and progress to satisfactory healing. One cause of failure is tension. A more common cause is infection of serum and blood accumulated beneath the flaps. Both can be avoided by preoperative evaluation of the wound, by careful hemostasis, and by the use of widely spaced sutures as provision for drainage. Tantalum or stainless steel wire which are ideal for sec-

ondary closure were not available. Hence, many wounds showed reaction around silkworm gut, silk, and, to a lesser extent, cotton sutures. Sulfanilamide crystals have not been used for local implantation at the time of wound closure. In those cases in which preoperative study of the wound flora revealed streptococci, the systemic administration of sulfadiazine and penicillin was continued into the postoperative period. These drugs were not given routinely. Pressure dressings were applied after operation, and extremities were immobilized and elevated. The importance of early and frequent inspection of these secondarily sutured wounds cannot be emphasized too strongly. They cannot be treated as fresh surgical wounds, covered and forgotten until it is time to remove sutures or until pain and rising temperature force inspection of the wound. The judicious removal of a tight suture, the evacuation of blood or serum, and the application of heat and wet dressings will salvage most of the small percentage of secondary closures that do not heal by primary intention. Failures resulted from undue tension on wound margins or from attempts to obtain cosmetic results with closely placed sutures.

In summarizing experiences with secondary suture after wound excision, it has been learned that this procedure must not be applied in certain anatomic sites where the skin is normally tense and where adequate mobilization of the margins of the wound is impossible. A high percentage of success has been attained by the use of loosely tied sutures, spaced widely enough to allow drainage, and by attention to the details of postoperative care. This method has been employed satisfactorily in the closure of defects left by drainage of abscesses and excision of carbuncles. *It must never be used when the skin and fat at the margins of the wound are indurated.* If this induration persists in spite of the use of heat, elevation, immobilization, pressure, and chemotherapy, the wound should be grafted or surgery should be delayed. Secondary closure performed in such a field will break down and the resultant wound will be worse than the original.

#### SPLIT-SKIN GRAFTING

*General Considerations.*—Split-skin grafts were used in the treatment of 306 patients. The most extensive procedure involved grafting of both lower extremities from the upper third of the thigh to the ankle. Fifty-two small grafts of the hand and foot are included. All size gradations existed between these extremes and multiple wounds were grafted in seventeen patients. This latter condition was seen most commonly in the forearm and leg where wounds of entrance and exit had been débrided widely or incised for drainage. Sixteen burn wounds which were grafted included three extensive phosphorus burns from chemical shells. Flash burns incurred as a result of the "Kamikaze" attacks on shipping were second degree burns and usually these were healed at the time of admission. A third degree burn of the helix of the ear is frequently a complication of this type of injury. There is great danger of chondritis and disfiguring deformity unless these areas on the auricle are grafted promptly. Thin Thiersch grafts were used to cover nine of these burns of the ears. These operations were done as procedures on the ward and are not included in the

analysis of split-skin grafts. Grafting was done in nine patients with ecthymatous ulcers. Elective excisions of scarred areas followed by skin grafting were done only when circumstances promised early return of the soldier to duty. Accidental wounds provided the opportunity for a small number of immediate split grafts to the fingers and hand. Choice of grafting procedures was based upon the principles set forth in a preceding section.

The number and character of wound complications which were met in the cases in which skin grafting was done are as follows: associated with fractures, 108 wounds; with exposed bone, 40 wounds; with exposed tendon, 38 wounds; with draining sinuses, 55 wounds; with pyarthrosis, 14 wounds, with clinical gas infection or gangrene, 43 wounds. Characteristic examples of complicated wounds are seen in Figs. 2 to 8. One or more of these complications often occurred in that same wound. Their presence precluded any consideration of



Fig. 8.—A, Gas gangrene of the arm following compound fracture of the ulna caused by bomb fragment. Photographs taken forty-eight hours after incision. B, Appearance of the arm two weeks after application of split grafts to the granulating wounds. Open-dressing technique as illustrated in Figs. 9 and 11 was used in this case.

secondary wound closure. In the majority of cases, split grafts were applied as a temporary procedure. Examples of such wounds are shown in Figs. 13 to 16. In others the split graft represented the reparative and the final steps in surgery. Examples are shown in Figs. 17 to 19.

Complete healing resulted in 265 patients, or 86.6 per cent, partial failure occurred in 21 grafts, or 6.9 per cent, complete failure in twenty instances, or 6.5 per cent. The efforts of beginners in operative surgery are included in this series of skin grafts and account for 35 per cent of operations performed. The causes of failure will be analyzed later.

*Methods.*—Split-skin grafts were cut freehand with the Ferris Smith knife in 291 cases. The Blair-Brown suction box was used to maintain skin tension. The Padgett dermatome was used in only fifteen operations. Dermatome grafts were selected for their uniformity and thickness when permanent results were desired. Cosmesis is not to be emphasized in reparative surgery. Donor sites were treated with petrolatum gauze and compression dressings. Bias-cut stockinet proved an efficient substitute for commercial elastic bandages. The

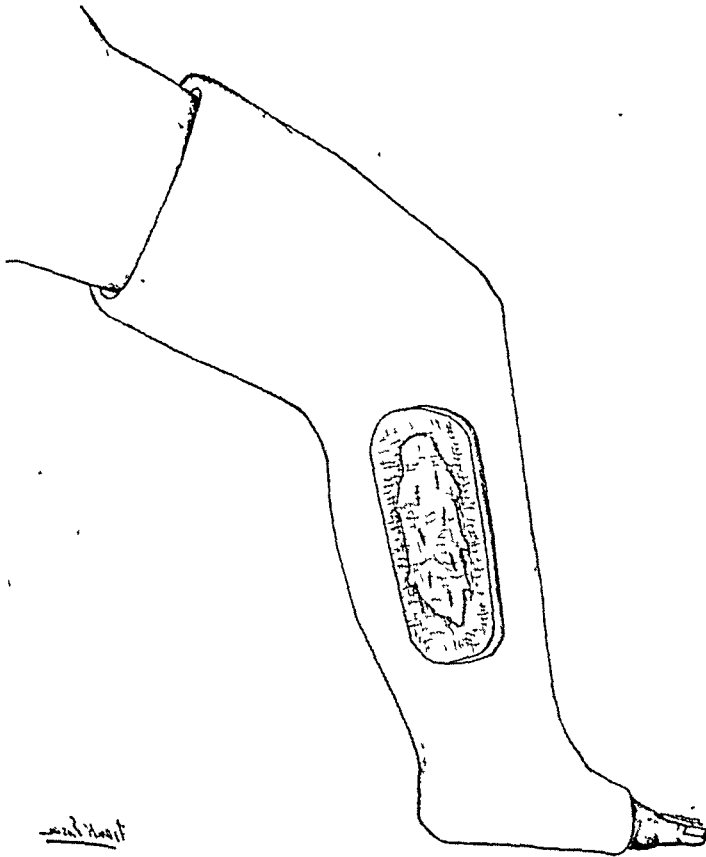


FIG. 9.—Open-dressing technique of split-skin grafting of granulating wounds as used in reparative war surgery. The perforated and patterned graft is securely anchored by the single layer of coarse gauze fixed to the surrounding skin by collodion. Sutures are unnecessary. The fibrin produced by granulations is adequate to fix the graft. Plaster cast immobilization was used. Window provides access for change of saline dressings. Immobilization and protection of the graft are essentials of postoperative care.

thigh was chosen for the donor area whenever conditions permitted. Scarred skin margins and excess granulation tissue were removed from forty-two wounds prior to grafting. This group represents about one-half of those wounds which probably did not need further reconstructive surgery. Grafts were applied directly to granulation tissue in early wounds. Granulation tissue was allowed to remain with conscious intent in many other wounds. Continued maturation and contraction of scar will reduce the size of the grafted defect and facilitate final steps in reconstruction. Tissue loss was minimal in these casualties from

the Phillipine Islands and grafts were usually applied for reasons other than the loss of skin and subcutaneous tissue. At the time of débridement in the forward areas, skin and subcutaneous tissue had been preserved whenever possible. The meticulous method of suturing the grafts in place and immobilizing them



FIG 10—A, Suspension of extremities by skeletal traction for the treatment of soft tissue wounds. Severe wounds of the right buttock, left thigh, and right calf. Cultures positive for *Cl. welchii*, *Kirschner* wire and stockinet with ACE adherent were used for suspension and grafts cut from the back. These were applied without sutures. Grafts were anchored with mesh gauze and collodion. Saline dressings were used. Bed and general care are simple with the use of skeletal traction. B, Result of application of multiple thick-split grafts. The patient had gained weight and was walking at the time he left for the United States.

by pressure was used only when dermatome grafts were applied. This time-consuming technique was replaced in 268 grafts with a more simple method. In this method the split graft is applied to the wound and held in place by a single layer of gauze mesh which in turn is anchored to the surrounding skin with collodion (Fig 9). Fixing agents as recommended by Sano were not used.

A wet sponge was used to moisten the gauze and stick it to the graft. The shrinking of the gauze as it dries increases the tension slightly. If necessary, the extremity is immobilized in plaster. The grafted area is exposed to the air for a period of two to six hours. Saline dressings are then applied and changed at four-hour intervals. The graft is open to inspection at any time. Should blood or serum accumulate it is simple to incise the graft and to evacuate such collections. Loss of graft from this source may thus be prevented. The



Fig. 11.—Suspension of extremities by skin traction in the treatment of wounds due to burns. Adhesive traction and open-dressing technique. The annular nature of the burns prevents use of windowed plaster cast in such cases.



Fig. 12.—Use of skin and skeletal traction and the open wet dressing technique in grafting third degree burns.



gauze anchorage is removed on the fifth or sixth postoperative day. If well moistened, it peels off without danger of separating the graft. Following this the graft is exposed to the air for increasing intervals of time. It is not neces-



FIG. 13.—A, Application of temporary dressing grafts. Loss of soft tissue and cartilage of nose. Granulation tissue grossly infected; much swelling and induration of surrounding tissue. B, Result of split grafting. In this case the graft was treated by the open-dressing technique as shown in Fig. 9. Note shrinkage of the grafted area and disappearance of edema. The site is ready for reception of a reconstructive flap.



FIG. 14.—A, Another example of the efficacy of temporary dressing grafts in reducing edema, preventing contracture and deformity, and preparing a site for reconstructive surgery. Appearance of wound of the face seven days after injury caused by Japanese anti-aircraft fire. B, Appearance after the application of a thick-split graft which serves as a temporary surface until reconstructive surgery can be carried out.

sary that the graft be trimmed to exact pattern. The excess may be draped over the normal skin at the margin of the wound. This may be trimmed off with the scissors when the collodion anchored layer of gauze is removed. Immobilization may be discontinued on the ninth to the twelfth postoperative day



Fig. 15—A, Anterolateral view of massive loss of soft tissue and three-fourths of the shaft of the humerus. Shoulder and elbow joints intact. Vessels to the forearm and hand preserved with function normal. B, View after split-thickness dressing grafts were applied before evacuation to the United States. The use of split grafts and the maintenance of length of the arm by plaster spica are steps in the reparative phase of the surgery of this case. The patient now is a candidate for reconstructive surgery involving soft tissue reconstruction by means of tubed pedicle and later massive bone graft.

and pressure dressing is then substituted if the patient is to be allowed out of bed. Plaster cast or splint was used for immobilization of 201 grafts applied to the extremities (Fig. 9). Casts were windowed for dressing changes. In some cases the grafting operation was done through existing windows. An ex-

tremity supported with skeletal or adhesive traction needs no other immobilization (Figs. 10 to 12). Such grafting may be done to great advantage while the patients are on the ward and their postoperative care may be reduced to the simplicity of dressing changes. Forty-three patients were treated in this fashion. Skeletal or adhesive traction for immobilization and protection of grafted areas is extremely valuable. When the grafts are applied to head, face, or thoracic trunk the collodion gauze anchorage provides sufficient immobilization. A bottomless cardboard box painted with collodion to render it waterproof or a wire cage taped to the face offers a convenient protection to the area and a container for the saline moistened dressings.

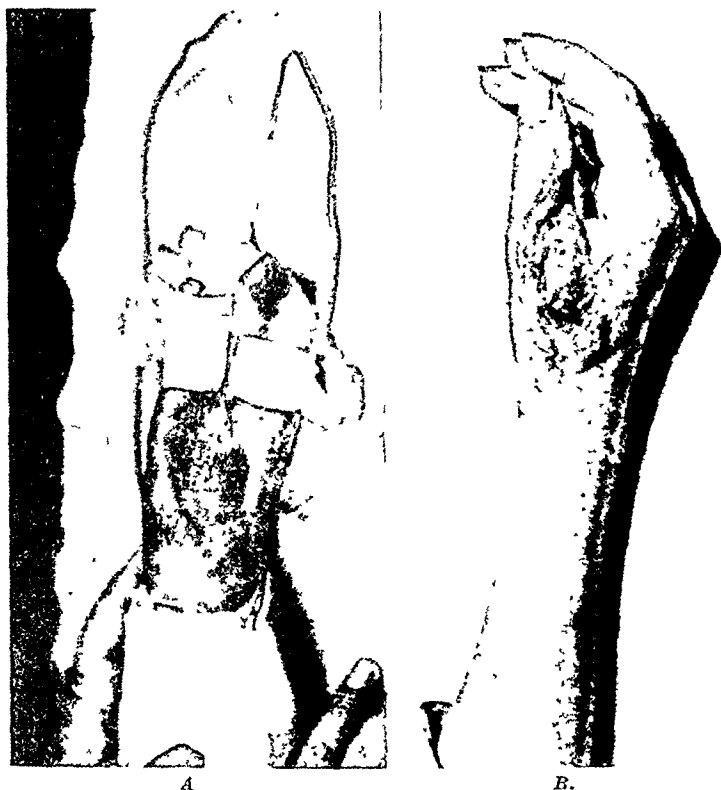


Fig. 16—A, Injury to thumb with loss of both extensor tendons and exposure of metacarpal and phalangeal bones due to enemy shell fragment. B, Result thick-split graft. Flexion, adduction, and abduction of the thumb were of the fact that bone and capsule of the metacarpophalangeal joint are directly under this graft, a pedicled flap will be needed when reconstructive surgery is done.

In summary, it may be noted that this open-dressing technique was directed toward economy of time and effort essential in war surgery. It was used in the treatment of 268 split grafts. Freehand grafts may be cut and the donor site dressed in the time which would be spent in adjusting the dermatome, applying cement, and waiting for it to dry. Suturing of grafts seldom is necessary in the reparative surgery of war wounds. Grafts should be inspected twenty-four hours after operation in order to remove collections of serum or exudate when necessary. This open-dressing technique for the postoperative care of split grafts makes it possible to cover successfully those complicated granulating

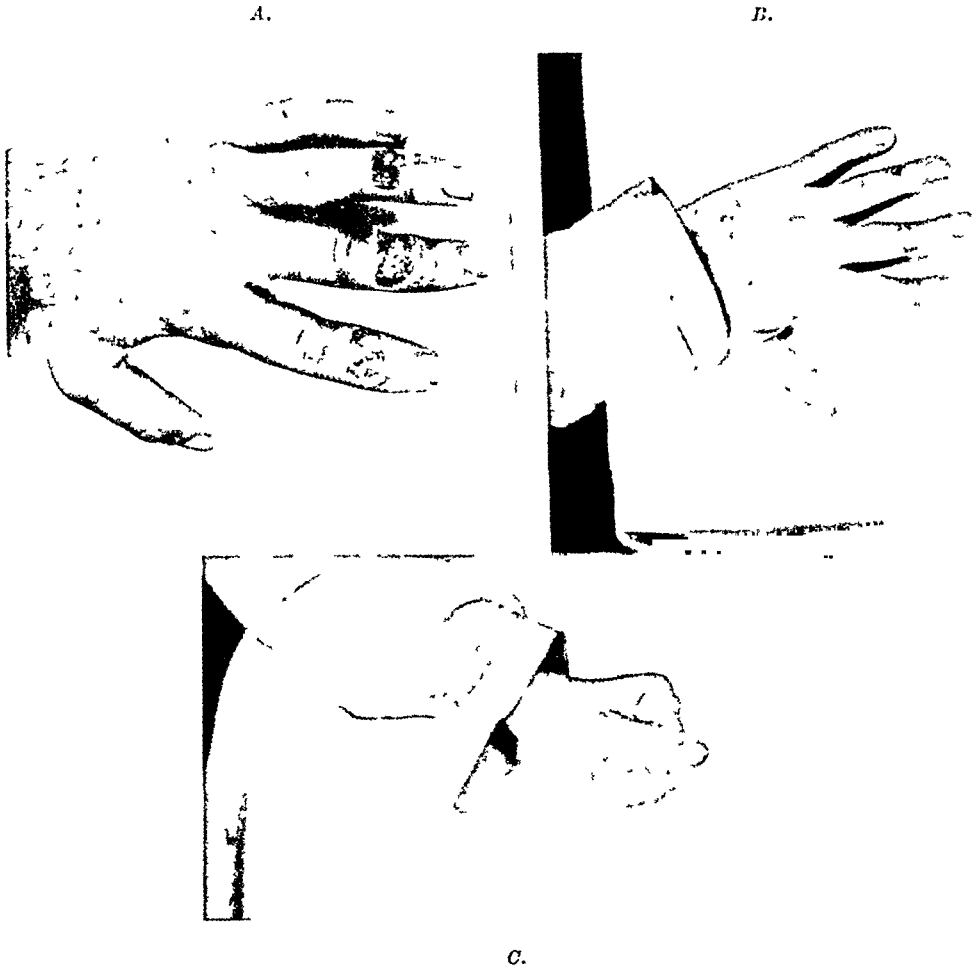
wounds which even may be inundated in pus draining from a fracture site or infected joint cavity. Buried coral fragments or cocoanut fibers are common in wounds sustained from mortar fire at beachheads. Removal of these multiple, minute foreign bodies would demand that the wound literally be combed. Grafts will take on such wounds and the superficial foreign bodies will later extrude through the graft. Such an instance is illustrated in Fig. 2. When treated by the open-dressing technique, grafts will take on exposed live bone and tendon if the periosteum or paratenon is intact (see Fig. 7).



Fig. 17.—A and B, Dorsal and ventral views of wound of penis showing annular loss of skin over the base and the proximal two-thirds of the penis C and D, Appearance after application of thick-split graft which was sutured in place Petrolatum gauze—adhesive tape immobilization was used, with indwelling catheter.

*Causes of Failure.*—The commonest causes of failure in skin grafting are neglect in considering the bacteriology of the wounds, errors in judgment in the proper selection of optimum time for surgery, and mistakes in technique or postoperative care, notably the failure to immobilize adequately a grafted area. Infection with beta-hemolytic streptococci was the largest single cause of complete or partial failure of split-skin grafts. Eleven complete and two partial failures were conditioned by this infection. Streptococci appeared in the wounds during

a rare and brief epidemic of upper respiratory infection that swept this base during late January and early February, 1945. During this period, bacteriologic facilities were unable to handle the large volume of work occasioned by the rapid influx of patients. Delay in receiving culture reports occasioned by this circumstance caused some concern. Choice of time for closure or grafting was based upon the appearance of the wound and the knowledge that streptococci are rarely found in the tropics. Streptococcal infection produced extremely



C.

Fig 18—A, Third degree burns of dorsum of three fingers with exposed extensor tendons. B, Result after application of thick-split graft to wounds; open dressing technique was used in this case. C, Photograph shows full flexion of damaged fingers following skin grafting, soldier returned to duty.

rapid liquefaction necrosis of the graft. Only the keratinized layer resists destruction. This is found floating on a layer of pus and cellular debris at the end of twenty-four to thirty-six hours. One large graft inspected six hours after its application to a phosphorus burn of the calf was found almost completely necrotized. The infection was controlled by systemic therapy with penicillin and a second graft applied eight days later with complete success.

Massive exudative infection due to *B. pyocyaneus* was controlled by the use of acetic acid dressings. However, it was demonstrated repeatedly that the presence of this organism on a granulating wound did not jeopardize the take of the graft when treated postoperatively by the open dressing technique.

In forty-three cases, wounds were grafted despite the fact that *Cl. welchii* had been recovered on culture. Forty of these perforated grafts were successful. There was complete failure in two and partial failure in a third. This experience has led us to the conclusion that wounds with anaerobic contamination may be healed by grafting. Secondary closure is contraindicated because of the danger of activating the anaerobic infection.



Fig 19—A, Grenade wound of foot twenty-eight days old at the time of admission of patient. B, Dermatome graft cut at 0.026 inch and sutured in place after excision of scarred wound margins and granulation tissue. Petrolatum gauze pressure dressing and plaster cast used. Result on the day of evacuation to the United States, sixteen days after application of the graft. In this case a generous proportion of the plantar pad had been preserved. Thick graft was applied in the belief that further reconstructive surgery would not be necessary.

In one instance the laboratory was late in reporting the recovery of *Corynebacterium diphtheriae* from an ulcer of the leg which had been grafted by the suture and pressure-dressing technique. Sixty thousand units of diphtheria antitoxin were given immediately. The dressings were not disturbed until the seventh postoperative day. Seventy per cent of the graft had undergone coagulation necrosis. The necrotic portion of the graft was firmly adherent to an underlying necrotic base. The appearance was identical with the necrotic base of cutaneous ulcers due to virulent *C. diphtheriae*. Partial or complete failure of split grafts to take over exposed bone or tendon occurred in five instances. These failures were ascribed to errors in surgical judgment. Inadequate immobilization accounted for one complete and four partial failures of grafts about

the shoulder, the axilla, and the abdomen. Hemorrhage caused partial failure in four grafts applied in combination with wound excision and partial secondary closure. Two failures resulted from errors in technique made by operators inexperienced in the use of the open-dressing technique. Collodion had been applied over the entire surface of the graft. Acute hepatitis with severe jaundice developed in two patients during the immediate postoperative period. Blebs of bile-stained serum collected under the grafts on the fifth postoperative day and partial loss of graft followed. An interesting wound complication developed in a patient convalescing from scrub typhus. Granulation tissue underwent hyaline coagulation necrosis. Eight-day-old small deep grafts which had been growing actively also underwent necrosis. No record of the cause of failure was kept in five other cases in which split grafts had been used.

This analysis shows that failure to consider the bacteriology of wounds as well as errors of judgment and mistakes in technique and postoperative care were responsible for the 6.5 per cent of cases in which split grafts failed. The fallacious legend that wounds heal poorly and that skin grafts are not successful in the tropics has been disproved. Lack of fresh foods in the diet and low blood vitamin C levels exerted no apparent influence upon the results. Vitamin C determinations were below normal (30 mg. per cent or less) in 57 per cent of 171 patients in whom vitamin determinations were done.

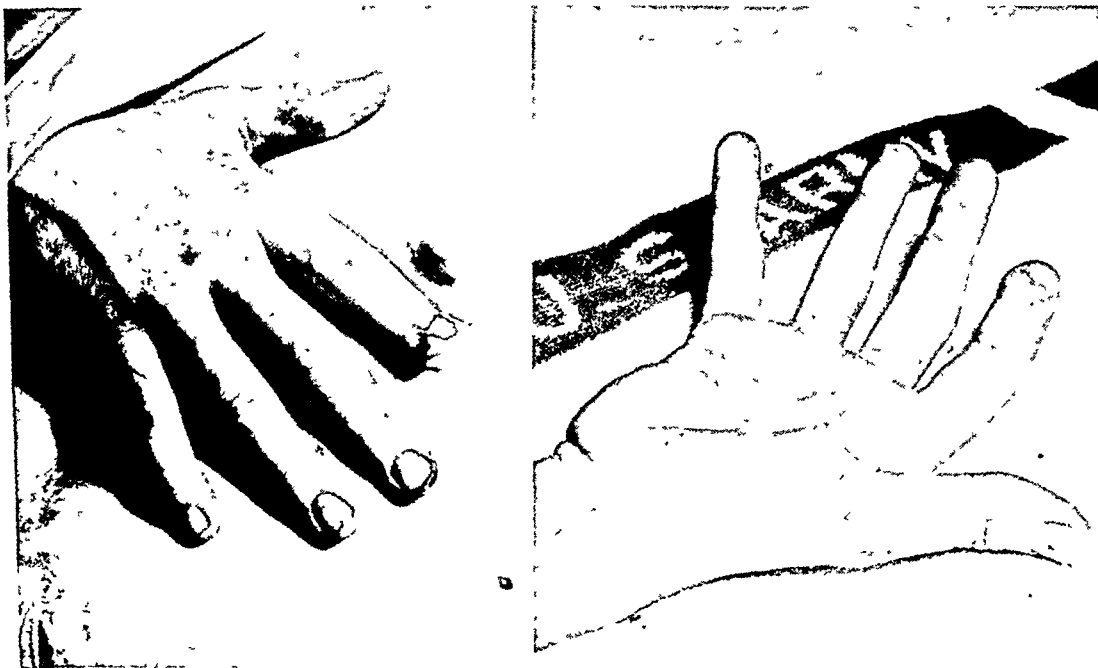
#### SMALL DEEP GRAFTS

Surgical literature is filled with condemnation of the use of the small deep grafts. However, we believe that these are very valuable in the treatment of certain types of wounds. These are the small, irregular, indurated lesions found in the groin, the popliteal area, the antecubital fossa, over bony prominences such as the malleoli, patella, acromion, olecranon, the foot, and the hand. Usually these are caused by bomb or shell fragments. They are not amenable to secondary closure and split grafts seldom are successful. Split grafts may take primarily but later they show a marked tendency to ulceration. Spontaneous healing is very slow and the resultant scar is atrophic and breaks down easily. A minor wound of this character may be responsible for prolonged disability. Small deep grafts were used in the treatment of forty-six wounds of this type. Excess scar and granulation tissue was removed. Deep grafts were cut approximately 0.7 cm. in diameter and placed as closely as possible to cover these small defects. They were retained in place by the mesh gauze and collodion technique as used in the treatment of split grafts. Saline dressings and occasional gentle saline irrigation to remove excess exudates are the features of postoperative care. Following the early take of the small deep grafts, complete epithelization of the wound is prompt as minimum space is left between the grafts. A pliable, thick covering is provided that will withstand cutaneous trauma equally as well as the thickest split grafts.

#### PEDICLED FLAPS AND TEMPORARY SPLIT GRAFTS

There are few occasions for the use of tubed or pedicled flaps during the intense activity of caring for large numbers of battle casualties. The overseas

general hospital can give neither bed space nor professional time and talent to such surgical procedures. Reparative plastic surgery has two primary objectives. The first is to return promptly to duty all military personnel who can give service within the theater. The second mission is to select for evacuation to the United States those patients who cannot be rehabilitated for duty within the 120-day hospitalization limit of military necessity. With these principles in mind, it should be emphasized again that the widespread use of split-graft dressing of wounds will protect the soldier from further scarring and deformity and return him prepared physiologically and anatomically for elective plastic reconstruction. The use of temporary grafts relieves the patient and professional attendants of the burden of dressing care in this intermediary period. Figs. 13 to 16 are examples in which temporary grafts have been provided in the reparative phase of surgery. On return to the United States, a soldier whose wound has been surfaced by a split graft may avail himself of convalescent furlough before reporting for reconstructive surgery.



A.

B.

Fig. 20.—A, Pedicled flap attached to finger-tip amputation. B, Following detachment of the flap the distal joint is preserved and a painless stump is assured.

An exception to this general principle is made in the case of fresh injuries of the hands and fingers. Wounds involving traumatic amputations of the portions of the fingers or other loss of tissue are frequent among personnel who work with mechanized equipment or who handle supplies. Every viable and recoverable segment of a finger should be saved. Reamputation proximally and the fashioning of a palmar flap for closure decreases the strength and function of the hand. Attempts to close these traumatic amputations frequently result in



tense, painful amputation stumps which ultimately may destroy the efficiency of the soldier. A small immediate flap from the opposite subpectoral area can be fashioned quickly and attached under local anesthesia. Such an example is shown in Fig. 20. The flap is detached, contoured, and sutured in place after establishment of circulation. This preserves all possible length and strength of the finger and gives a cushioned painless stump. Occasionally an injury of the foot may be salvaged for duty by the use of a pedicled flap from the opposite calf. A small per cent of facial wounds can be closed with sliding flaps. This same principle has been used in repairing defects over bony prominences applying a split graft at a distance from the original wound. Z plastics have a place in reparative surgery in the correction of mild contractures. Variations of the procedures mentioned make up the group of twenty-eight plastic operations previously listed as primary procedures involving the manipulations of flaps of skin and subcutaneous tissue.

#### SUMMARY

An analysis is presented of the activities of the plastic surgery section in a large general hospital where battle casualties are received from tropical areas. Such activities are directed largely to the early obliteration of wounds by secondary closure or skin grafting in order to prevent further scarring and deformity. This reparative or intermediate surgery conserves the resources of the patient and sends him to the United States prepared for final reconstructive surgery. Experiences in the treatment of 848 patients serve as a basis for this report. The responsibilities of the plastic surgeon include the supervision of wound care and the selection of the time for operation as well as the choice of operative procedure. The long lines of communication in the Pacific area imposed additional problems in reparative surgery of the wounded. Older wounds are less suitable for secondary closure. Skin grafting rather than secondary closure was used in a higher percentage of cases as the time interval between injury and admission to this hospital increased. Principles guiding the decision as to the use of secondary closure or skin grafting in the treatment of war wounds have been discussed. Tropical climate has been found to influence only the phase of preoperative treatment. The problems are primarily dermatologic. In the postoperative care of grafts frequent changes of wet dressings give results superior to closed-dressing techniques. Tropical wound flora have been studied. It is noteworthy that streptococcal infection is uncommon. This is explained by the rarity of upper respiratory disease in the tropics. Organisms other than streptococci did not interfere with the successful outcome of reparative plastic operations. Local use of sulfonamides and penicillin have been of little value in this series of wounds treated in the tropics. The advanced age of wounds at the time of admission has necessitated wound excision as a preliminary to secondary closure in many cases. Attention to the avoidance of tension, careful hemostasis, widely placed sutures, the use of postoperative immobilization, elevation, pressure, heat, and wet dressings was rewarded by ideal healing in a high percentage of cases. Split-skin grafts were reserved for those cases in which there was loss of tissue or in which there were mechanical

complications in the wound. In the majority of cases these split grafts were employed as a temporary measure in preparation for later constructive surgery. In others the split graft represented the reparative and the final steps in surgery. A detailed discussion is given of the open-dressing technique of split-skin grafting. With this technique we have achieved a great economy of time and effort and only 6.5 per cent of 306 grafts have been complete failures. This method has been taught successfully and quickly to a group of medical officers with no previous experience in plastic surgery. An analysis of the causes of failure in grafting has shown that these are due to failure to study the bacteriology of wounds, to errors in surgical judgment, or to mistakes in technique and post-operative care. No basis was found for the legend that wounds heal poorly in the tropics. Low blood vitamin C levels produced no detectable influence on results of reparative plastic operations. Small deep grafts have been used to our complete satisfaction in the treatment of small fibrotic wounds in certain locations. There are few occasions for the use of pedicled or tubed flaps in an overseas general hospital. The management of battle casualties from the Philippine Islands provided experience with recent and late war wounds of all types. Due to circumstances of distance and the strategic location of hospitals in the Southwest Pacific Area, the general hospital has provided a laboratory in which the reparative phase of plastic surgery has had an unequalled opportunity for development.

## THE COAGULUM CONTACT METHOD (SANO) OF SKIN GRAFTING IN THE TREATMENT OF BURNS AND WOUNDS

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THE early covering of large granulating surfaces by skin grafts is of the utmost importance. This is true whether the injury is due to burns or wounds. Due to unavoidable difficulties in transportation from the forward area, a period of one to six weeks usually elapsed between the time of injury and admission to our hospital. During this interval it was inevitable that some infection of the large granulating areas should occur. Grossly these appeared in good condition, but cultures taken from them showed multiple organisms, the more frequent of which were *Staphylococcus aureus* hemolyticus and streptococcus with beta hemolysis, often overgrown with *Bacillus proteus*. The problem of covering these denuded areas by skin grafting was urgent, both to control infection with its associated dangers and to prevent subsequent contractures of the involved areas. The technical difficulties of securing a complete take under such conditions are well known. Therefore, it was decided to use the coagulum contact method of skin grafting described by Sano,\* since it offered an opportunity to observe the graft continuously.

This method has been used in 120 instances, 38 patients being operated upon while the hospital was located in Australia, and the latter 82 while the hospital was on an equatorial island with all patients in tent wards. Forty-two of the patients required skin grafts because of third degree burns, while the remaining seventy-eight individuals had defects of varying sizes due to wounds. On the whole, the general condition of those patients who had been wounded was far superior to those who had been burned. This was in spite of extensive supportive measures, such as the giving of plasma, supplying a high protein diet, and supplementing the vitamin intake.

In the early cases the method described by Sano was followed exactly. However, this was soon modified, particularly the postoperative care of the grafts. In brief, the following procedure has been followed in all cases. The plasma and cell extract solution have been prepared by the Laboratory Service.† A kit which includes the following items is autoclaved for this procedure:

- 1 10 c.c. syringe
- 2 23 gauge needles
- 2 20 gauge needles
- 4 Centrifuge tubes with corks
- 1 Wassermann tube with glass beads and cork
- 4 Capillary pipettes

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\*Sano, M. E.: A Coagulum Contact Method of Skin Grafting as Applied to Human Grafts, Surg., Gynec., & Obst. 77: 510-513, 1943.

†Under the direction of Lieutenant Colonel Joseph H. Bragdon, Medical Corps, Army of the United States.

Approximately one hour before the scheduled time of the operation, 10 c.c. of blood is drawn from the patient under aseptic conditions. Sufficient heparin is used to wet the barrel. It is felt that an excess of heparin should be avoided. The heparinized blood is then placed in a sterile centrifuge tube which is centrifuged, and the plasma, or solution "A" is then pipetted off and placed in a sterile tube. The "buffy coat" is then pipetted off and placed in 2 c.c. of Tyrodes solution in the Wassermann tube, which is shaken in a Kahn shaker, and then centrifuged. The clear supernatant fluid is then pipetted off into another tube and is solution "B" or the "cell extract." The plasma and cell extract are then delivered to the operating room for the use of the surgeon.

The preoperative preparation of these patients is of the utmost importance. The granulating areas were covered with dressings kept moistened with a solution of  $\frac{1}{3}$  per cent sulfanilamide and  $\frac{1}{2}$  per cent acetic acid, the latter controlling pyocyanus infection which is prevalent in this area. On the day before operation saline dressings were substituted and these were changed frequently to prevent accumulation of exudate. Complete blood studies were made on these patients. In case of anemia, transfusions were given and where a low serum protein was found, plasma was given until a normal level was obtained. Also, an attempt was made to secure a high vitamin C intake as an aid to tissue healing. Since it was impossible to sterilize completely the granulating area, penicillin was used routinely. Two days before grafting, penicillin was started by the intramuscular route; 100,000 units were given during each twenty-four hour period, the dosage being 12,500 units every three hours. This was continued on the day of operation and for the two subsequent days so that penicillin therapy extended over a period of five days. At the time of operation penicillin was also used locally.

The donor area was prepared with tincture of green soap, alcohol, and ether. All grafts were cut with the Padgett dermatome, using in most instances a thickness of .015 inch. It was found that the use of a thin paste of sulfanilamide powder facilitated the removal of the graft from the drum and also the glue from the surface of the donor skin. The recipient area was irrigated with saline solution and then blotted with sponges, care being taken to prevent bleeding. The area was then completely covered with a film of penicillin solution of a concentration of 5,000 units per cubic centimeter. This was allowed to dry. After removing the graft from the drum, the reverse side was covered with the film of the "cell extract." At the same time the recipient site was covered with plasma. The graft was then immediately placed on the recipient area, taking care not to move or slide the graft after it was applied. Pressure was applied by means of forceps in order to secure good contact. In our experience the graft was firmly adherent within a few minutes. In those patients in whom there were large defects, such as burns involving the entire lower extremity, the procedure was frequently performed in two stages. In the first stage, grafting was done on the anterior aspect of the extremity, and one week later the same procedure was carried out on the posterior aspect. In this length of time, the grafts placed at the first stage had taken well, and

the patient could be placed on the abdomen without danger of injury to the graft. Such a program always kept the new grafts upper most, and prevented any exudate from passing downward and perhaps floating them off.

Early it was found that the application of even a single layer of boric ointment gauze tended to cause the accumulation of exudate beneath this, particularly in the area surrounding the graft. Therefore, this procedure was eliminated and no dressings were applied. The areas grafted were protected by either a cradle or the use of a mosquito net over the entire bed. In the case of burns where there were granulating areas surrounding the grafts, there was a tendency for crusts of dry serum to heap around the grafts. Because of this the grafts and surrounding areas were sprayed every two hours beginning six



Fig. 1.—Split-thickness graft applied on seventh day following gunshot wound; appearance of graft on first postoperative day. (Courtesy of United States Army Air Force.)

hours after operation. Either the sulfanilamide-acetic acid solution or normal saline solution was used. After two or more days, constant wet saline dressings were used to cover the entire area. Strict observation of the graft was necessary. In those grafts in which there was an overlapping, the graft was trimmed on the second postoperative day so that the entire excess was removed. There was frequently a loss of the superficial epithelial layer and it was found that as it became loosened it should be excised. This method is far from foolproof. It was found that unless attention was paid to these postoperative procedures there would be a partial loss of the graft. It means that inspection of the area must be made at least twice a day and the necessary measures taken.

The areas grafted varied in size from small skin defects 4 to 5 cm. in diameter to those requiring four to five drums (32 square inches per drum). Since penicillin has been used routinely as described, there has been an increase in the percentage of complete takes. There were five cases in which there was total loss of the graft, one of these in a patient whose injury was due to burns, while the remaining four were in patients that had granulating



Fig. 2.—Six days after grafting; there is more loss of superficial epithelium than in average case. Complete take at end of three weeks. (Courtesy of United States Army Air Force.)



Fig. 3.—Four weeks after grafting; large wound with considerable loss of underlying muscles. (Courtesy of United States Army Air Force.)

areas following wounds. In nine cases only 50 per cent of the graft remained viable, while in twenty-two cases, 25 per cent of the graft was lost. In the remaining eighty-four cases there was a complete take or at least a negligible loss along a portion of the periphery of the graft at its junction with normal skin. In all instances these defects were covered with epithelium within a few days. Because of the necessity of evacuation it has been difficult to follow



Fig. 4—Split-thickness grafts applied to area following third degree burns, grafts on left are four weeks and those on the right two weeks after grafting. Complete take at end of eight weeks (Courtesy of United States Army Air Force.)



Fig 5—Homogenous grafts (dark areas) surrounded by autogenous grafts, thirty days after grafting.

these patients and thus determine the late results. A few that have returned to this hospital six months or more following grafting have shown an excellent condition of the graft with a good cosmetic appearance.

In one patient, sufficient skin was not available as a donor site due to extensive areas involved and on three different occasions homogenous grafts using three different donors were placed, following the method described. After determining that the donor and recipient were of the same blood type and were completely compatible, blood was drawn from the donor and used to obtain the plasma and cell extract required in this procedure. The patient was a Negro but his skin was very light in color. Two of the donors were white men and the third a very dark Negro. The first graft was applied on March 2, 1944, and was  $2\frac{3}{4}$  inches by  $1\frac{3}{4}$  inches; the second donor supplied three grafts each 4 by 8 inches in size, which were placed March 21, 1944; and May 25, 1944, an area 9 by  $3\frac{1}{2}$  inches was covered with skin from the third donor. When last seen before evacuation the grafts were in excellent condition and had been in place for 110, 91, and 27 days, respectively. In a follow-up letter it was reported that the first graft disappeared rapidly in a few days beginning July 15, 1944, the second grafts disappeared at the end of July, and the third graft the early part of August. This gave a survival time of roughly 135, 130, and 75 days, respectively. When the patient was seen by one of us three months later it was found that the areas had healed without further grafting being required, apparently from the growth of epithelium from the surrounding skin beneath the grafts. The other grafts, which were numerous and which had been taken from the patient's own skin, were all completely viable at this time. While these homogenous grafts were ultimately failures they more than fulfilled their purpose, for early covering of the denuded areas was possible and also the final result has been most satisfactory.

There are certain disadvantages in the use of the coagulum method, the chief of which is the contracture of the graft when applied and, therefore, a greater donor area must be available. Since there is no suturing to keep the grafts under tension they tend to contract when applied to the recipient area. Where there is only a limited area available for a donor site, this must be considered. Where the cosmetic appearance is of importance it is our impression that the results are not as good as when the graft is sutured to the surrounding skin, in which case the line of union is less noticeable. However, it has certain factors which are of importance in its favor. It permits grafting to be done rapidly and this is important in a military installation where many casualties may require operative treatment in a brief period. It is of special value in large granulating areas such as those associated with burns where suturing is difficult. Another group of wounds in which we have found it of special use are those in which it is difficult to place a pressure dressing such as on the neck overlying the trachea and in the gluteal folds. The end results were more uniformly successful when this method was used to cover areas of third degree burns than when used to cover those of wounds. In the latter



there frequently was an ingrowth of epithelium which caused a peripheral loss of the graft and some scarring.

#### SUMMARY

The modifications of the Sano coagulum contact method of skin grafting have been discussed, and the use of penicillin as a valuable adjunct in skin grafting is presented. The procedure can be performed without difficulty in an institution which has the usual laboratory equipment. It has been found to give good results and while it may not supplant the classical methods, there are certain cases in which it is the method of choice.

# THE PLASTIC CORRECTION OF SUPERFICIAL VASCULAR AND PIGMENTED NEVI

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NEVI may be classified in two groups: vascular and pigmented.

## VASCULAR NEVI

Vascular lesions can be subdivided further into the capillary and cavernous types. Each variety may be found anywhere on the surface of the body and there is no limit as to the size to which either may grow.

The capillary variety is ordinarily known as a strawberry or port-wine mark, depending upon the shade of color it may present. As with other nevi, the etiology is unknown except that they may be congenital anomalies. Histologically one observes an overgrowth of dilated capillaries and connective tissue in the skin substance.

While dermatologic treatment should always be considered, the scope of this series of cases deals only with the surgical repair. The former therapy ordinarily consists of repeated applications of carbon dioxide snow or properly calculated doses of radium or x-ray therapy. The aim in either method is to attempt to produce an obliteration of the dilated capillaries and thereby lighten the color to match the adjacent normal skin. This functions well in the simpler lesions, but with the more complicated variety, even the dermatologists admit that complete cure cannot be obtained because the amount of treatment needed may produce necrosis and subsequent scarring, a complication worse than the original tumor.

For this more complicated group of cases, and those in which judicious conservative dermatologic treatment has been only partially successful, excision of the lesion should be carried out and the resulting cutaneous defect closed by undermining and suturing the adjacent skin edges or by applying a properly selected skin graft. In certain cases, I have followed the plan advocated by Smith,<sup>12</sup> that is, removing the lesion in multiple stages accompanied by the use of Z plasties when indicated, and suturing the divided skin edges after wide undermining. This results in a fine hairline scar, which of course is always preferable to a skin graft when the method is applicable since it insures a cosmetic result that most closely matches perfection.

The cavernous tumors consist of swollen masses of large dilated venules or veins. They are frequently more difficult to eradicate since they are likely to be deep seated and extensive. Their size may progress with age, so that the earliest treatment will insure the best results. Neglect may also predispose to ulceration and infection. Rupture and severe hemorrhage are not uncommon.

Large cavernous angiomas may be well treated by surgical excision. Because of their great vascularity, operation often should be preceded by the injection of sclerosing fluids, partial ligation, or exposure to radium or x-rays. This will produce sufficient fibrosis so that the mass can be resected without too much danger from hemorrhage.

As with the capillary nevi, the resulting skin defects are closed either by undermining and suturing the adjacent skin flaps or by the substitution of a properly selected skin graft. It should be pointed out that the resulting cutaneous defects that follow the excision of large nevi, sears, etc., must often by necessity be closed at once with a skin graft. Many of these defects can be markedly improved at later operations by excision of all or part of the graft and then suture of the skin borders after wide undermining. This procedure adds to the finesse of the final result but can be accomplished only by time and patience on the part of both the surgeon and patient.

#### PIGMENTED NEVI

The pigmented nevi are brownish colored lesions which vary in shade from tan café au lait to the deeper brown colors. Contrary to popular belief, the large or giant brown growths rarely seem to have the malignant tendencies that we were all taught to expect. However, those which border on the darker shades should be looked upon with a great deal more respect since this type is more likely to take on malignant changes. The size varies from that of a small mole to several hundred square inches in area. Hair may or may not grow out from their substance. The etiology of pigmented nevi has never been solved although some individuals feel that they may be congenital malformations.

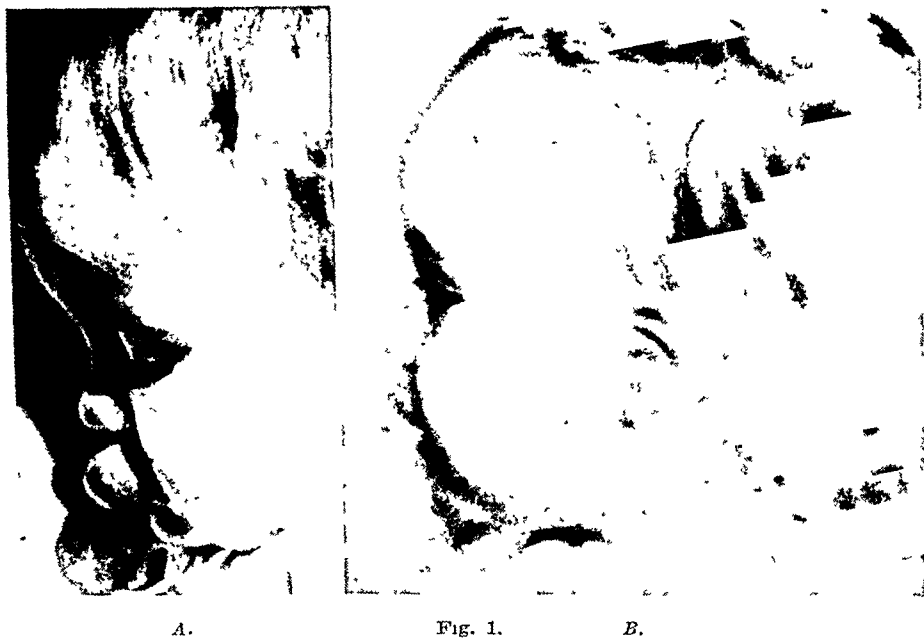
There is considerable difference of opinion as to the pathologic classification of these tumors. Most of them are of epithelial origin, but there is evidence to show that some may be of mesoblastic derivation. A few are angiomatous in nature, which makes their treatment more complicated. While the majority of the lesions are benign in character, certain ones, and these are usually the smaller tumors, degenerate into melanoblastomas or melanosarcomas. Chronic irritation may be a factor in the production of this change.

For the sake of safety, expediency, and best cosmetic results, pigmented nevi should be excised. Except possibly for small lesions of lighter color and which are clinically of the nonmalignant type, the use of physical agents such as cauterization, fulguration, radiotherapy, etc. should not be employed. All deep-colored nevi should be excised widely and the adjacent skin edges closed. As with the hemangiomas, the larger tumors may be removed by multiple excision and suture or, if this is impossible, the resulting cutaneous defect may be replaced with a properly selected skin graft. Whether or not the giant nevi should be removed in toto or in part over repeated stages depends largely on the size of the individual lesion. The time consumed in surgery and the amount of blood loss, even with transfusions, may preclude complete removal of certain giant growths in a single operative session. Obviously then, better surgical judgment dictates that these should be managed in stages.

For illustration, the foregoing considerations are elaborated by Cases 1 to 17.

## CASE REPORTS

CASE 1 (See Fig. 1, *A* and *B*).—A 1-year-old child presented a large growing cavernous hemangioma of the upper lip. This lesion would be subjected ordinarily to irradiation but for economical reasons, the parents, who lived several hundred miles away, could not bring the child back for repeated treatments. As an alternative, it was elected to remove the mass surgically. This was done through an intraoral incision through the mucous membrane of the upper lip. The swelling was readily dissected out, the vessels ligated, and the wound closed with interrupted catgut sutures. A rapid and uneventful convalescence followed and the patient was discharged from the hospital eight days later.



CASE 2 (See Fig. 2, *A* and *B*).—A cavernous hemangioma in the left nasocanthal fold was treated with radium in infancy. Too much exposure was given, which resulted in a thick fibrotic scar and damage to the underlying bony epiphysis. This was untouched during the period of growth, so that the left side of the nose was held back while the right side continued to grow normally. A marked asymmetry of the nose resulted. To correct this problem, it was necessary to shift the entire nasal bony framework back to the midline, apply a free full-thickness skin graft over the defect created in the left nasocanthal line, and build up the left ala with a pedicle flap from the forearm. This was truly a major undertaking as compared with either excision of the hemangioma or obliteration by a dermatologist trained in the judicious use of radium.

CASE 3 (See Fig. 3, *A* and *B*).—A capillary hemangioma had been present since birth. The patient had prolonged dermatologic treatment consisting of irradiation and applications of carbon dioxide snow. While considerable improvement followed, the patient was not satisfied and had grown very self-conscious of the discoloration.

This strawberry mark was removed in multiple stages, with complete undermining of the facial and neck skin at each operation. As much of the nevus was removed in each of two operative procedures as could be done safely without suturing the skin under too much tension. At a third stage the suture line was revised so that all that remained was a fine linear inconspicuous scar running parallel to and just below the ramus of the mandible.

As with many cosmetic defects, the eradication of the mark in this adolescent girl produced a striking psychologic change.



CASE 4 (See Fig. 4, A and B).—This port-wine nevus in a 20-year-old girl is of interest in several different respects. Before coming to us the patient had had a long series of treatments with carbon dioxide snow and then radium. In fact, the lesion was complicated by a mild radiodermatitis when we first saw her. The notching in the left ala was due to a healed ulcerative reaction to radium.

The first operation consisted in removal of all the lesion except that involving the left upper and lower eyelids. The defect was then covered with a primary thick split-skin graft. At a later date the eyelid skin was removed and replaced with a single free full-thickness skin graft taken from behind the ear. This latter graft was chosen for the eyelids so that the maximum amount of lid function might be anticipated.

An excellent result with the eyelids is noted. In contrast, however, the thick split-skin graft has not yielded an equally satisfactory result, even though marked improvement over the original lesion must be admitted. It is hoped that the patient will return to permit removal of the split-thickness graft from the cheek. This can be done by a combination of multiple excision and suture plus a Z-plasty to prevent the formation of an ectropion of the lower eyelid. The nasal graft should be exchanged for a free full-thickness graft and the ala defect corrected by the method of Kazanjian.



A.

Fig. 4.

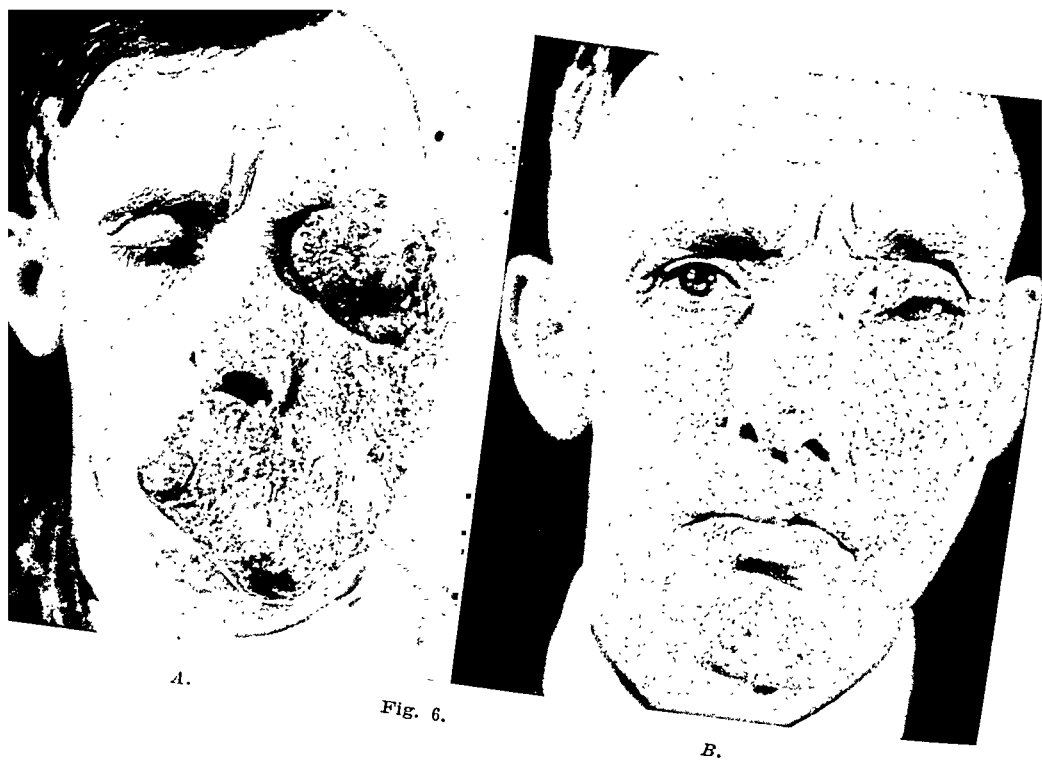
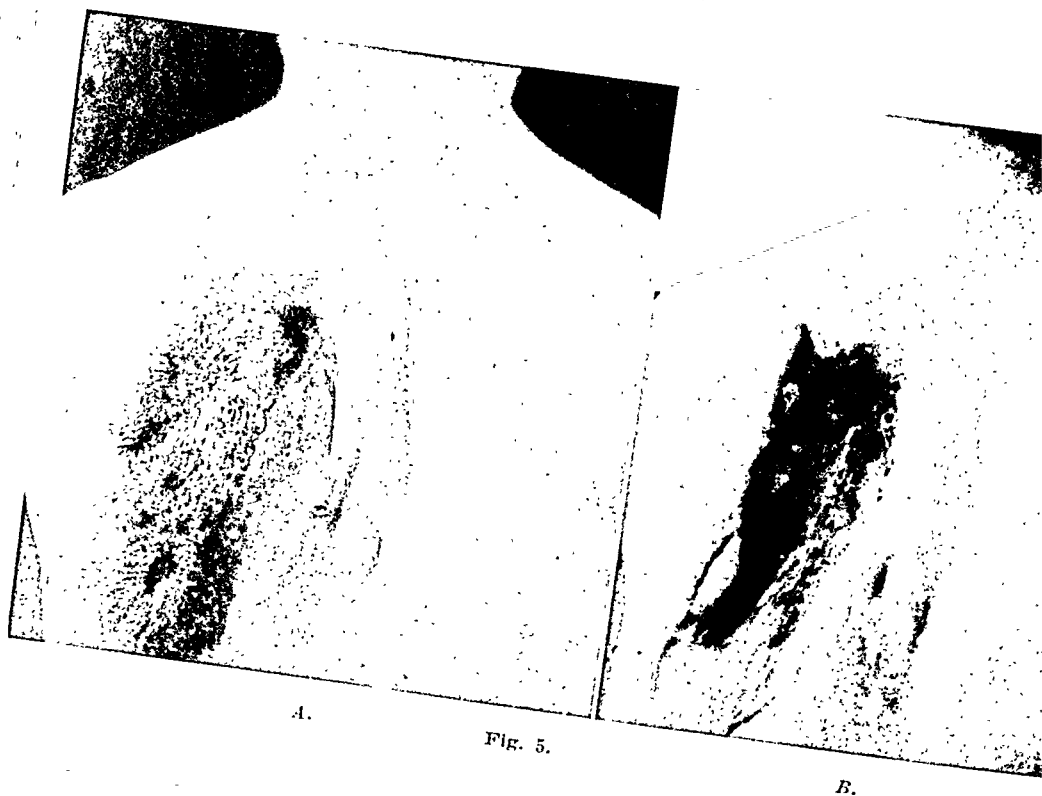
B.

CASE 5 (See Fig. 5, A and B).—A girl had a large cavernous hemangioma of the back that had caused trouble all her life. Hemorrhages were the most annoying complication. She had had large doses of radium and x-ray therapy but only with moderate improvement.

Dr. de Takats injected many of the larger vessels with sclerosing fluids and later resected the entire mass. Owing to hemorrhage it was necessary to pack the wound and permit it to granulate. Three weeks later, two large split-skin grafts were cut and placed over the open wound.

CASE 6 (See Fig. 6, A\* and B).—A man 36 years of age when sent in to us, gave a history of a small cavernous hemangioma arising from the left cheek. His parents said that it was first observed when he was six months old (at which time it could undoubtedly have

\*FIG. 6A from De Takats: *Diagnosis and Treatment of Cardiovascular Disease*, F. A. Davis Company.



been eradicated easily by radium). No treatment was given and the mass continued to grow progressively. Occasional complicating hemorrhages occurred from the rupture or erosion of a vessel. He sought treatment elsewhere during recent years but was always turned away because of the magnitude of the tumor.

The patient first came under my observation six years ago. The left cheek and upper lip were composed essentially of a large mass of dilated veins which extended through the mucous membrane, back over the soft palate, and down the throat as far as one could see. Obviously the patient was not a good candidate for operation until the mass was adequately prepared in advance of surgery. Therapy was complicated by the enormous size and vascularity of the lesion, which unfortunately can be ascribed to neglect.

I am indebted to Dr. de Takats for the early treatment of the patient. His first step was to ligate and divide the external carotid artery just above the origin of the superior thyroid artery. This resulted in a marked reduction in size of the tumor. Then followed a long series of injections of sclerosing fluids. The excess of the mass was then resected and the remainder given massive doses of deep x-ray therapy. At still a later date the cheek and upper lip were revised. The vessels in the eyelids were removed by excision.

While this cannot be considered a perfect result, it is a great improvement and the patient has subsequently married.



A.

Fig. 7.

B.

CASE 7 (See Fig. 7, A and B).—A 19-year-old girl had a large papillary hairy pigmented nevus of the right cheek and nose. It had remained the same since birth and no previous treatment had ever been attempted.

The lesion was removed in one operation and replaced with a primary free full thickness skin graft taken from the inner aspect of the upper arm. A complete "take" occurred. Being a graft of full-thickness skin, it will take cosmetics well. The sections did not reveal any malignancy.



CASE 8 (See Fig. 8, *A* and *B*).—A child, 7 years of age, had an elevated benign hairy pigmented nevus of the nose and inner canthus of the left eye. The preoperative photograph (Fig. 8, *A*) was taken after several months of treatment with carbon dioxide snow. The growth was removed in one operative session and the resulting defect replaced with a primary free full-thickness skin graft taken from the inner aspect of the upper arm. It was interesting to note that upon discharge the child commented, "Now the other children will not call me pig-face!"



A.

Fig. 8.

B.

CASE 9 (See Fig. 9, *A* and *B*).—A 19-year-old girl had a very extensive verrucous pigmented hairy nevus. It had been present since birth but had shown no change in size except as it grew in proportion to the rest of the body. Her parents sought surgical consultation several times but were always sent back with the opinion that the growth was inoperable. As a compromise she was treated for many years with local applications of carbon dioxide snow but with only slight improvement.

At a later date the patient was referred for plastic surgery. The entire mass was removed in five divided operative sessions, spaced approximately three months apart. Each operation was accompanied by considerable blood loss, which was corrected by immediate post-operative blood transfusions which had been planned in advance. The skin defects were covered with large primary intermediate-thickness skin grafts. A little fibrosis developed beneath some of the grafts but this is rapidly disappearing with the aid of x-ray therapy which is being given by the dermatology department.

In no sections of the removed tissue was any malignancy found.

It is quite obvious that this patient now has a completely different outlook upon her future.

CASE 10 (See Fig. 10, *A* and *B*).—A 5-year-old boy had a disfiguring hairy pigmented nevus involving nearly all of the left half of his face. He was also developing a striking psychosis at this early age, which we felt was due to the facial deformity.

Because a large skin covering would be needed and since some areas would be difficult to immobilize, it was felt that the defect could best be covered by using a tube pedicle flap.



A.



B.

Fig. 9.



A.



B.

Fig. 10.

This was elevated from the left mastoid process down to the left pectoral region. When the flap was ready for transfer, the tumor was excised and the lower end of the flap, which had been designed to the same size and shape as that of the tumor, was removed from the chest and sutured into the facial defect. The pedicle was divided two weeks later. The cheek flap needs to be readjusted at a subsequent date.

The sections showed no evidence of malignancy. It was also interesting to note the changed psychologic reaction of this young patient after the operation.

4

B.

C

D

E

F

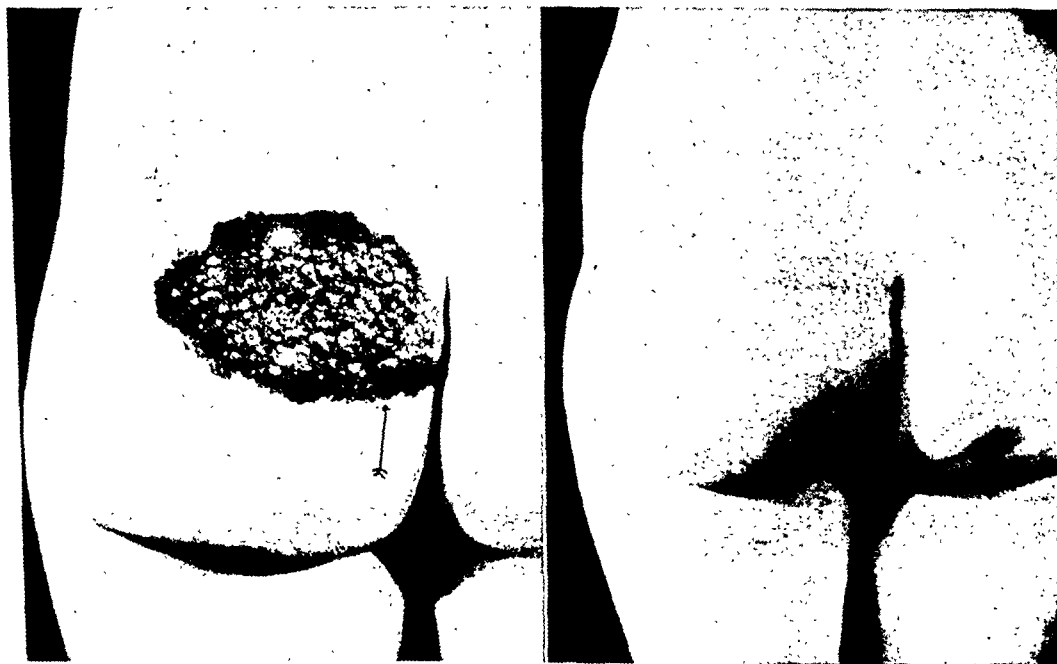
Fig 13



A.

FIG. 14.

B.



A.

FIG. 15.

B.

blastoma arising from the pigmented nevus. In view of this, the patient was examined for metastasis but none have been found in the two years that have followed operation. Deep x-ray therapy was given over the operative site for empirical reasons.

CASE 16 (See Fig. 16, A and B).—A Negro woman, aged 32 years, is included in this series because the therapy used represents a mistake due to the misleading report of a biopsy.

# RAYON, AN IDEAL SURGICAL DRESSING FOR SURFACE WOUNDS

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THE conception of fundamental principles of wound healing, in the light of modern physiologic research, has undergone marked change during the past few years. As a result, many worth-while revisions in routine treatment have been suggested. One of these has been the pressure dressing, today commonly accepted in the treatment of burns and large surface wounds. This therapy has been adequately described by numerous authors,<sup>1-3</sup> but one important component part of the pressure dressing which deserves more study is the material placed in immediate contact with the wound.

Discussion on this subject has been controversial and there exists a variety of opinions regarding the proper material for this purpose. Many surgeons are still of the opinion that the ideal dressing for placement in immediate contact with a wound is fine mesh gauze (44 by 40) impregnated with some nonirritating type of grease, such as petrolatum or merthiolate ointment. Siler<sup>4</sup> (used gauze impregnated with petrolatum or hydrous wool fat; Prioleau,<sup>5</sup> gauze impregnated with petrolatum; King,<sup>6</sup> allantomide ointment overlaid with petrolatum gauze; Strange and Mourot,<sup>7</sup> gauze impregnated with 6 per cent sulfanilamide in equal quantities of cold cream and lanolin. Gurd, Ackman, and Smith<sup>8</sup> packed the interstices of the wound, from the depths outward, with gauze impregnated with 5 per cent sulfathiazole emulsion. For an initial dressing, Whipple<sup>9</sup> used fine meshed gauze or tulle gras impregnated with an ointment or solution. Gurd and Gerrie<sup>10</sup> shingled the surface of the burn with Nottingham lace buttered with sulfathiazole emulsion.

A number of constant factors have been found which reflect unsatisfactory healing when ordinary dressings have been used: pain and discomfort, excessive bleeding, delayed healing, and interference with drainage where grease dressings have been applied. It is felt that these factors are reflections of the types of materials which have been used for immediate contact with the surface of wounds. Pain and bleeding seem to be related to the open mesh of the ordinary dressing, since the mesh is sufficiently wide to permit the penetration of capillary buds. As a result of this capillary penetration, the newly formed blood vessels have been torn when dressings were changed. Friction frequently develops between dressings and wounds when a coarse material is used in immediate contact with a wound. Because of this, grease dressings have been used in an effort to diminish irritation, pain, and delayed healing.

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The ideal dressing for immediate contact with the wound should conform to certain physiologic principles: it should be easily sterilized; it should be of a weave sufficiently close to block the entrance of capillaries into the substance of the fabric; it should permit adequate drainage; and it should have a low coefficient of friction, thus reflecting a minimal irritation to the underlying wound. Experiments were designed and numerous fabrics were used in an effort to obtain a material which would fulfill these requirements. Following considerable experimentation with various materials, nylon was tested in October, 1943. After observing many applications of this material, results appeared to be satisfactory in some respects, but nylon failed to fulfill all of the physiologic requirements enumerated.

Shortly after this, experimentation with rayon was conducted. (Rayon is a fabric woven from a glossy fiber made by forcing a saponified solution of cellulose acetate through minute holes and drying the filaments in air or chemicals.) An attempt was made to determine the fineness of weave which would be required to block the entrance of capillaries, presuming the diameter of the smaller type capillary to be around 8 to 9 microns. A very fine weave of approximately 114 by 114 was used for the initial experiment with rayon. This material proved satisfactory for, upon removal of the dressing, it was found that there was little disturbance to the underlying granulation and a gratifying diminution of pain and bleeding was noted. In attempting to evaluate more accurately the diminution of capillary permeability into the rayon, paraffin blocks of portions of rayon and of fine mesh gauze were made. From these blocks, sections were cut and mounted for microscopic examination. Studies of these sections revealed that capillaries penetrated the open mesh gauze, while the weave of the rayon was sufficiently fine to prohibit entrance of the capillary buds into the substance of this material in most instances. Bleeding and pain are constant factors following the removal of a surgical dressing when open mesh type of material is used. Pain and bleeding were markedly reduced when the rayon was used in preference to a fine mesh gauze and patients were grateful for the great diminution of pain. Rayon showed permeability which permitted adequate drainage; in no instance was it felt that the drainage was blocked. When used under a pressure dressing, a granulating tissue was produced which appeared smooth, red, and velvety. Reduction of infection was apparently facilitated by the use of this material.

The rayon and nylon, used in these experiments, were moistened with normal saline solution or 2 per cent acetic acid, buffered to a hydrogen-ion concentration of 4 with sodium acetate, before being applied to the wound. On no occasion was grease used. No sulfonamide drugs were used as this investigation was directed toward a study of the dressing material and its evaluation.

As a result of these experiments, I feel that rayon is an ideal material for contact with burns, granulating areas, surface wounds, and donor sites where skin grafts have been removed. The size of the fiber in the material chosen is 30 denier. The number of threads, warp and weft, is 114 by 114. The thickness of the cloth is .0020. This material has the same tendency to burn as any material made of synthetic or chemical yarns.

## TECHNIQUE OF DRESSING

The technique required for the inclusion of rayon in the application of a pressure dressing to a *surgically clean surface wound* varies only in the substitution of the rayon for the fine mesh gauze originally described.<sup>3</sup> A single layer of rayon is applied to the surface of the wound, and only this material is moistened with saline solution or 2 per cent acetic acid buffered to a hydrogen-ion concentration of 4 with sodium acetate. The material is tailored to fit the wound. If it is necessary to encircle a limb, not more than one inch of the rayon is to be allowed for overlapping because a double thickness of the fabric may interfere with drainage. When applying rayon in contact with an infected wound, the entire dressing is rendered slightly moist, otherwise the secretions from the wound have a tendency to become dry. If this is permitted to develop and a moist capillary-drainage type of dressing is not constantly maintained, the wound is sealed effectively and drainage is blocked. When rendering the dressing moist, capillary drainage is established between the wound and the substance of the dressing, thus preventing unnecessary absorption from a puddling of secretions. Following the application of rayon to the surface of a wound, a regular pressure dressing, previously described,<sup>3</sup> is applied.

When removing the dressing from a *noninfected wound*, it is advisable to moisten the rayon with a bit of ether. Thus the sebaceous material, which frequently dries between the dressing and the noninfected wound, is dissolved and the dressing literally falls away with no adherence whatever. There is little complaint from the patient when ether is used in this manner. The margins of wounds are routinely cleansed with ether even though the edges are granulating. When removing a moist capillary-drainage type of dressing from an infected wound, this difficulty is not encountered because the moisture in the dressing prevents adherence.

In conclusion, investigation and clinical use, for a period of two years, have shown that rayon is an ideal material for dressings in immediate contact with any surface wound. It fulfills the physiologic requirements for an ideal material to be placed in immediate contact with a surface wound: permits adequate drainage; reduces friction with the wound to a minimum; prevents capillary invasion as a result of the fineness of the weave; and reflects a great reduction of pain and bleeding when dressings are changed. It is easily sterilized and withstands autoclaving, thus simplifying preparation for its use.\*

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# THE USE OF SALINE SOLUTION, GLYCERIN, AND ACETIC ACID IN THE CARE OF BURNS

## AN ODORLESS METHOD OF TREATING BURNS

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BURNS offer one of the toughest problems for the Navy surgeon of any problem he must face. Conditions aboard ship and conditions at advanced bases make standardization of burn treatments impossible and impractical. The results of the original treatments given burns in a forward area or aboard ship can never be viewed by the doctor who began the treatment. In each center where the burn is seen, the treatment of choice of the medical officer in charge is used, or the treatment that may be available at that time for burns. By the time patients with burns reach a base hospital or another large center, many of them have had two or three types of treatment, such as petrolatum gauze, sulfonamide drugs, dyes, tannic acid, paraffin sprays, or nothing. The standardized treatment advocated by the Bureau of Medicine and Surgery is petrolatum gauze with pressure dressings. The first problem facing the medical officer at a base hospital is how to clean off the various types of medications which have been applied to the burn, and how to control the infection which is invariably present. A treatment to do both these things has been developed, which is simple and easily applied.

Wet dressings were used in treating many infected and uninfected burn cases at a mobile hospital following the New Georgia and Vella La Vella pushes during the battles of the Solomon Islands. At first normal saline solution was used, which helped to remove previous applications, gangrenous sloughs, and exudates. As many of the burns were infected with *Bacillus pyogenes foetidus*, acetic acid 1.5 per cent was added to the saline solution. It was found that the foul odor usually associated with burns disappeared in one to two days after starting the saline solution-acetic acid dressings. Because of the difficulty in removing adherent dressings, glycerin was added to the combination. Various concentrations of glycerin and acetic acid were used, and finally 15 per cent glycerin and  $\frac{1}{2}$  per cent acetic acid in normal saline solution was found to be the most effective and least irritating of all the combinations tried.

The treatment here described is not a panacea for the treatment of burns and requires a lot of hard work. It does not take the place of blood studies and the intelligent use of plasma and whole blood transfusions. During the acute phase of the burn, daily checks must be made on the blood count, hematocrit, and plasma proteins. Fluids must be given at a rate of 5,000 c.c. daily with adequate whole blood in the early stages; when this is done there are fewer complications. This treatment is also not intended to eliminate the use of sulfonamide drugs or penicillin, both of which are very important. Recently the chemotherapy used has been 20,000 units of penicillin, intramuscularly, every

The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

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three hours. Sulfonamide drugs are used only if the patient cannot tolerate the penicillin.

In order to standardize the treatment, certain things had to be done first to bring all cases to the same footing. All burns and all slowly healing flesh wounds were immediately put on the following routine: (1) Discontinuance of all sulfonamide drugs and other therapy, (2) forced fluids, (3) full diet, (4) complete blood work, urine examination, and other indicated studies, and (5) redressing of all burned areas immediately. Whole blood transfusions were given by preference even though the hematocrit was high. Plasma was given when whole blood was not available. Sulfonamide drugs were not readministered for many of the patients had been given an overdose, which was probably due to the incomplete records that accompanied the patient from one center to another.

The dressings were applied as follows. Sterile three-inch gauze bandage with the finest mesh available was placed on an applicator stick by putting the applicator through the center of the roll of bandage. Moistened with a solution of normal saline, 15 per cent glycerin, and .5 per cent acetic acid (pH about 3.8) which had been previously autoclaved, the three-inch bandage will adhere easily to the burned surface. An arm or leg must be dressed by applying the first strips of narrow mesh gauze longitudinally. This will prevent constriction of the member should swelling and edema develop. As soon as the entire burned area is covered with the fine mesh gauze, five or six layers of heavy gauze are added, that packaged in twelve-inch rolls being the best. This may be dispensed from a long applicator just as the three-inch bandage. After these have been applied, they are moistened with the saline-glycerin-acetic acid solution until they are dripping wet. ACE bandages are then applied for pressure, beginning at the toes or the fingers and proceeding upward to cover the entire extremity, whether burned or not. The ACE bandage should not be wrapped too tightly, for when it becomes moist it will shrink.

The ACE bandages are removed every eight hours at which time the heavy gauze bandages underneath are remoistened with the saline-glycerin-acetic acid solution, and the ACE bandages reapplied. This procedure of moistening the dressings is carried out for nine or ten days, when the entire dressing is changed for the first time. At that time sloughing tissues of the third degree burns will begin to separate and will be ready to remove. No radical débridement is done in an acute burn and only those areas of skin which have separated are removed when the original dressing is done. Blisters are not opened and removed. Following the first dressing change on the ninth or the tenth day, it may be necessary to change the dressing every three days to remove additional sloughing tissues. The entire slough of an extensive third degree burn can be removed easily by the eighteenth day. Adequate narcosis can be maintained by  $\frac{1}{2}$  gr. of morphine, to be used only during the dressing changes. Further narcotics are not needed.

To change the dressing, the ACE bandages must be removed and, with a pair of sterile bandage scissors, the heavy twelve-inch gauze which has been previously moistened is cut through. With the slightest help, the cut bandage will drop away from the small mesh gauze lying directly on the burn. At

this point, another moistening of the gauze will aid in its removal. The fine mesh gauze is removed by pulling each strip separately, longitudinally and not transversely. There is less pain when the dressings are removed in this manner. Sedation should be employed until all of the slough of a third degree burn has been separated from the area. Sedation is not necessary at any time but at the dressing change.

Penicillin, 20,000 units every three hours, is continued until all second degree burns are healed or until the entire sloughing area of third degree burns has been removed. The use of sulfonamide drugs has been discontinued unless the patient is sensitive to penicillin or supplies of penicillin are not available. It is believed that there is less toxic effect on the kidneys from penicillin than from sulfonamide therapy.

The wide publicity heretofore given the sulfonamide drugs has made every man in the service and most civilians believe that the sulfonamides are the answer to all infections. They have certainly helped to overcome many bad infections that were never adequately treated before. This does not make it mandatory that all of us fall into a false feeling of security about the sulfonamide drugs. The same can be said about penicillin. They are of unquestioned value when used internally to control the systemic effects of infection, but I feel that sulfonamides and penicillin applied locally to the burned areas definitely slow the healing process. The more nearly physiologic can be made the local treatment for burns, yet holding infection in check, the better are the results.

Epithelization has been so rapid with this management that only the worst of the third degree burns have needed grafting. Three hundred and fifty-eight burns of all types and degrees have been treated; of this number, 231 had some third degree areas. The 127 second degree burns healed spontaneously in from seven to twenty-one days, without scarring of a disfiguring nature. Of the 231 third degree burns most healed spontaneously, only 18 needing skin grafts. One extensive third degree burn was allowed to heal in for experimental purposes when grafting would have speeded recovery; although both legs were burned from the shoe tops to the knees (third degree) they healed in 105 days under this management (Case 1).

#### CASE REPORTS

CASE 1.—A Negro man, aged 20 years, was burned with gasoline on Sept. 6, 1944, when a blowtorch exploded within a closed room. About 40 per cent of his body was burned with second and third degree burns. The face, backs of both hands, both forearms, both upper arms, both legs, thighs, and the right buttock were involved. Treatment was started elsewhere with partial débridement, plasma, and pressure dressings with petrolatum gauze. He was admitted to the service with a temperature of 105° F., badly in need of fluids and whole blood. The fluid balance was corrected and wet dressings, using the saline-glycerin-acetic acid solution were applied. There was an immediate drop in the temperature, which did not exceed 102° F. for the remainder of his time in the hospital.

Healing was allowed to take place in this patient without the benefit of grafting so that we could follow the epithelization. Both lower legs had extensive third degree burns going entirely around the leg. All of the skin sloughed and part of the subcutaneous tissue separated when the slough was removed. All of the burns of the hands, arms, thighs,



Fig. 1.

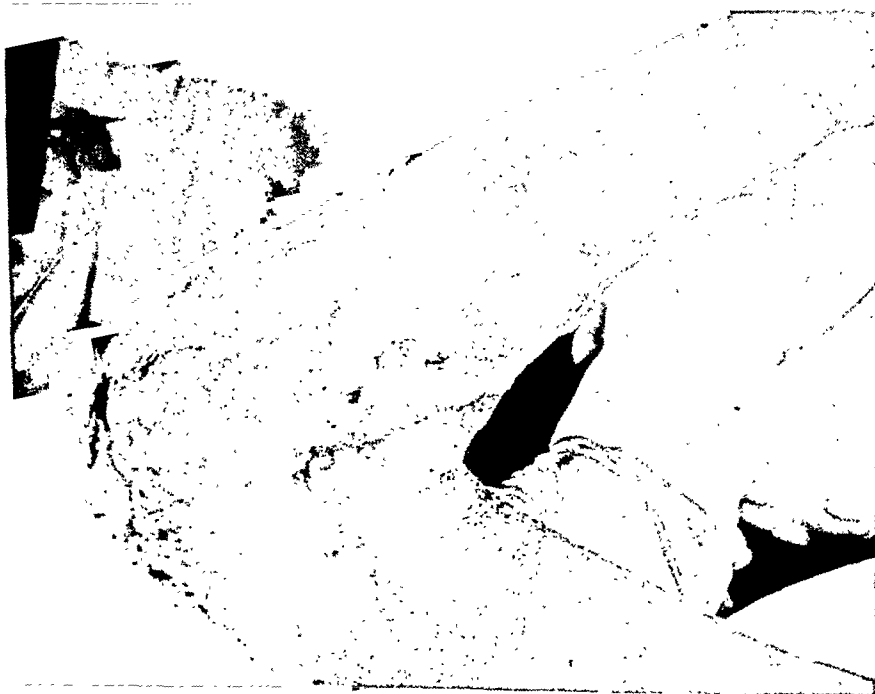


Fig. 2.

Figs. 1 and 2.—Typical infected third degree burns that have healed spontaneously under this management.

buttocks, and face were healed by the twenty-eighth day. This comprised about 90 per cent of the burned area. The remaining part took an additional 75 days to heal, thereby making a total of 105 days for complete healing of the entire burn without grafting.

CASE 2.—A 28-year-old white man was burned while cleaning a boiler. Superheated steam entered the boiler causing extensive second and third degree burns involving the



A.



B.

Fig. 3.—A, Infected third degree burn prior to grafting with seed grafts (Ravaden). B, One week following application of the grafts.

face, ears, neck, all of the back down to the belt line, the chest to the nipple line, both shoulders, both arms down to the hands, and both legs down to the shoes. About 70 per cent of the body area was involved. Immediate treatment consisted of  $\frac{1}{2}$  gr. morphine and the washing of the entire burned area with ether to remove oily substances applied before the patient arrived on the service. Skin that was loose from rubbing of clothes and from his efforts to get out of the boiler was removed. None of the blisters or obvious third degree areas were removed. The continuous pressure dressings with the saline-glycerin-acetic acid solution were applied. Whole blood was given, five transfusions, and two units of plasma in the first four days. The first dressing change was made on the ninth day. At that time about 80 per cent of the entire burn was healed. Successive dressing changes were made on the fourteenth, twentieth, and twenty-seventh days. The entire burn was healed, with residual scarring only on the third degree areas by the twenty-seventh day.

The patient, characteristic of all burn cases handled, was allowed out of bed on the tenth day and encouraged to become ambulatory as soon as he desired. At no time was there any kidney complication and there was not the usual secondary anemia found with severe burns. Penicillin was given at the rate of 20,000 units every three hours from the day of admission until the twentieth day. Narcosis consisted of morphine, gr.  $\frac{1}{2}$  the first day and gr.  $\frac{1}{4}$  for the first two dressing changes. The patient was without pain except for a slight stinging sensation when the dressings were moistened. The stinging sensation disappeared in two to three minutes after application. At no time was there any odor from the burn.

The most demoralizing thing about a burn ward is the odor which has been invariably present. The patients are apathetic, and it is apparent that the odor from the burns causes much of the poor morale found on the usual burn ward. This treatment kills all odors within twenty-four to thirty-six hours. It is most dramatic to have a new draft of patients with burns arrive on the ward; invariably they are most odorous. The acetic acid-glycerin-saline solution dressings stop the odors so that soon the new patients are laughing and joking as those in any clean surgical ward. Patients with extensive burns treated immediately with the acetic acid-glycerin-saline solution never develop any odor during the course of their treatment.

#### SUMMARY

1. A series of 358 burns have been treated with saline-glycerin-acetic acid solution, pH about 3.8.
2. The odor from burns is eliminated and the patients' morale is as high as in a clean surgical case.
3. There is no maceration of the tissues with this solution such as is common with petrolatum gauze and other ointments.
4. Glycerin in the solution, being hygroscopic, tends to make the dressing changes easier and apparently stimulates epithelization.
5. Acetic acid, even in such small concentration, provides an adequate check upon the pyrogenic infections.
6. These dressings clean the burns very rapidly, resulting in clean granulating surfaces suitable for early skin grafting.
7. Doing the dressings without anesthesia makes it possible to avoid part of the danger of a complicating pneumonia.
8. The very minimum of grafting is necessary under this regime, and epithelization appears to be faster than with other methods.

## THE USE OF ACETIC ACID-GLYCERIN-SALINE SOLUTION IN SKIN GRAFTING

LIEUTENANT FREDERICK E. LUDWIG, MEDICAL CORPS, U.S.N.R.

SKIN grafting has long been one of the most important procedures associated with burns and other slowly healing wounds. The results from grafting have been as variable as there are different individuals working with the problem. Anyone who works with burns or with slowly healing battle wounds must do some type of grafting. In the large series of burn cases recently reported,\* this method of grafting was employed for those cases that needed grafting. This method was also used when clean, retracted scars were excised prior to grafting and other slow-healing battle wounds.

There are certain important factors that must be controlled before grafting can be a success. The following procedures were followed in detail in all of the cases listed in Table I.

1. Grafting was not attempted until the hemoglobin of the blood stream reached the level of 80 per cent. Sufficient transfusions were used in all cases to achieve this level.

2. Preliminary dressings to clean the area to be grafted, using the acetic acid .5 per cent, glycerin 15 per cent in normal saline solution (ph about 3.8) with continuous wet pressure dressings, were applied in the same manner as the dressings for the acute burns. Severe burns are always ready to graft just as soon as the slough has separated, usually by the sixteenth to the eighteenth days.

3. The donor site is prepared with a forty-eight hour preparation using green soap the first day followed with ether and alcohol. Merthiolate or other mercurial agents have not been used on the donor skin, the two-day preparation with ether and alcohol being sufficient.

4. Ollier-Thiersch grafts have been used in preference to other types, the grafts being taken with the razor technique rather than with the dermatome. Donor skin is treated with great care so that the cut edges do not touch any surface other than the granulating area to be grafted.

5. While the operator is taking the graft under local anesthesia an assistant cuts off the pressure dressing from the site to be grafted and removes any obvious pieces of slough, dirt, or dressing that appear on the surface. It is not necessary to scrape the granulations, for the pressure dressings have kept them from overgrowth. The donor skin is then applied, using extreme care to prevent any of the edges of the new skin extending over any previously epithelized area. All wrinkles in the graft are smoothed out and all air bubbles that may have been caught under the graft are extruded.

6. Fixation of the graft is done by applying the burn dressing over the graft without suturing of the donor skin. Fine mesh three-inch gauze moistened in the acetic acid-glycerin-saline solution is placed directly on top of the grafted

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\*Ludwig, F. E.: The Use of Saline Solution, Glycerin, and Acetic Acid in the Care of Burns, *SURGERY* 19: 486, 1946.

TABLE I

TYPE OF CONDITION	NUMBER OF CASES	TYPE OF GRAFT	RESULTS—
			AVERAGE TAKE (PER CENT)
Burns, all classes	17	Ollier-Thiersch	90
Burns, all classes	2	Ravaden seed	70
Contracted scars from burns	4	Ollier-Thiersch	95
Infected wounds (amputations, compound fractures, etc.)	5	Ollier-Thiersch	70

area. Five or six layers of heavy rolled twelve-inch gauze is placed over the grafted site and moistened with the solution until dripping wet. ACE bandages are then applied to give continuous pressure on the graft. The ACE bandages are removed every eight hours, the dressings remoistened, and the ACE bandages reapplied. It is important that the dressings be kept wet for the succeeding seven days. The entire dressing is then removed for the first time, using care that all of the three-inch gauze is well moistened before any attempt is made to remove it.

7. Penicillin, 20,000 units every three hours, was given intramuscularly for seven days after grafting to inhibit infection. None was used on the burn or the grafts.

At the end of seven days the results of the grafting will be fairly obvious. The thin edges of the graft will take slowly while the centers will be well advanced by seven days. The same wet dressings are then reapplied until all of the ungrafted areas have bridged over.

Various types of dressings, grafts, and procedures were used in the development of this technique. Ravaden seed grafts were tried on two patients who had such severe burns that donor skin could not be found in patches large enough to use the Ollier-Thiersch method. Most of the seed grafts took (70 per cent) but it was found that many of them pulled off with the dressing changes due to their small size. Suturing of the graft to the wound was tried but it was found that occasionally the removal of the sutures on the eighth or tenth days caused a stitch abscess under the new skin. Fixation with the pressure dressings has been adequate. Fixation of the grafts with fraction A human plasma\* was used with fair results but with less success than with the acetic acid method (see Case Report).

Four recent burns (three to six months old and all healed) had markedly contracted anticubital spaces, hands, and axillae. These have been grafted with this method by the simple procedure of cutting away all of the offending scar and applying the half-thickness grafts to the subcutaneous tissue. About 95 per cent takes were noted in all of these clean cases. Extension of the elbow was improved from 90 to 160 degrees. Abduction of the shoulder was improved from 0 to 100 degrees. The two patients with fingers and the dorsum of the hands involved obtained 60 per cent of their normal motion from a complete fixation and a diminution of the webbing between the fingers. The end results of this method are not as good as those from tube grafting; however, this method

\*Lederle Laboratories, Inc., Pearl River, N. Y.



saves the patient many months of treatment and with the cooperation of the patient an adequate result can be obtained. It is too soon to be certain that the scarring will not return in the form of keloids later. Some contraction has been noted on two of these patients after four months, although the current results are much better than the original condition of the patient.

#### CASE REPORT

A white man, veteran of the United States Army, was admitted Dec. 1, 1944, with numerous third degree burns over both hands, forearms, upper left arm, and left shoulder. About 10 per cent of the body area was involved. This patient was epileptic and in a convulsion he fell onto a hot radiator. He was treated elsewhere with picric acid ointment and without débridement. As soon as he was admitted to the service, his burns were washed with ether to remove the ointment, and the saline-glycerin-acetic acid solution was applied as the wet pressure dressings. The burns were very deep with subcutaneous tissue involved so that sloughing continued for twenty-five days. At that time there was a noticeable ingrowth of epithelium. The bed of granulations filled in sufficiently so that on the thirty-eighth day there was a good bed of granulations upon which to graft. On the fortieth day half-thickness Ollier-Thiersch grafts were taken from the thigh and applied.

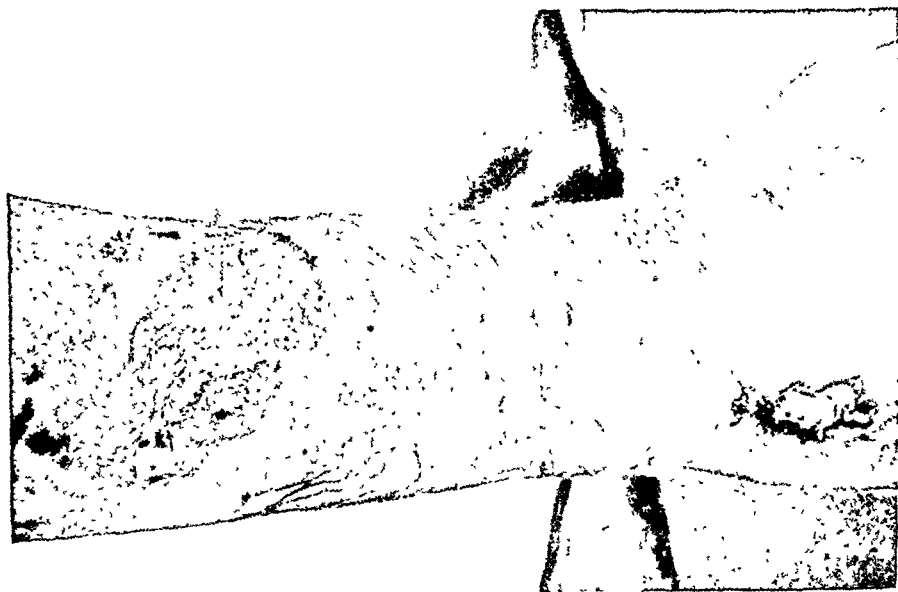


Fig. 1.—Back of right forearm grafted with half-thickness Ollier-Thiersch grafts placed upon a base of fraction A human plasma. There was an estimated 50 per cent take of the graft at the first dressing change on the seventh day postoperative.

For experimental purposes the right arm was treated with the human plasma fraction A and the grafts glued with the plasma. The grafts were held in place with perforated cellophane (since discontinued) and the usual burn dressing. The same technique of taking the graft, covering it with cellophane, and using the burn dressings was followed on the left arm except that the plasma fraction was omitted. Both arms were moistened for one week and then both dressings were changed. The right arm (plasma treated) showed about a 50 per cent take of the grafts. It was noted that the thin edges of the grafts failed to grow while the thicker centers survived (Figs. 1 and 2).

The left arm showed remarkably good results with about a 95 per cent take of the grafts on the lower arm (Fig. 3). On the upper arm the dressings slipped a little and

dried out so that there was only about an 80 per cent take of the graft. The small burn on the left hand was not grafted and was allowed to heal spontaneously to act as a control for the other two methods of fixing grafts. There was little healing although this small burn was dressed with the wet pressure dressings.



Fig. 2.—Seven days after the underside of the right forearm was grafted with the plasma fraction as the base. Here again about 50 per cent of the grafts survived.

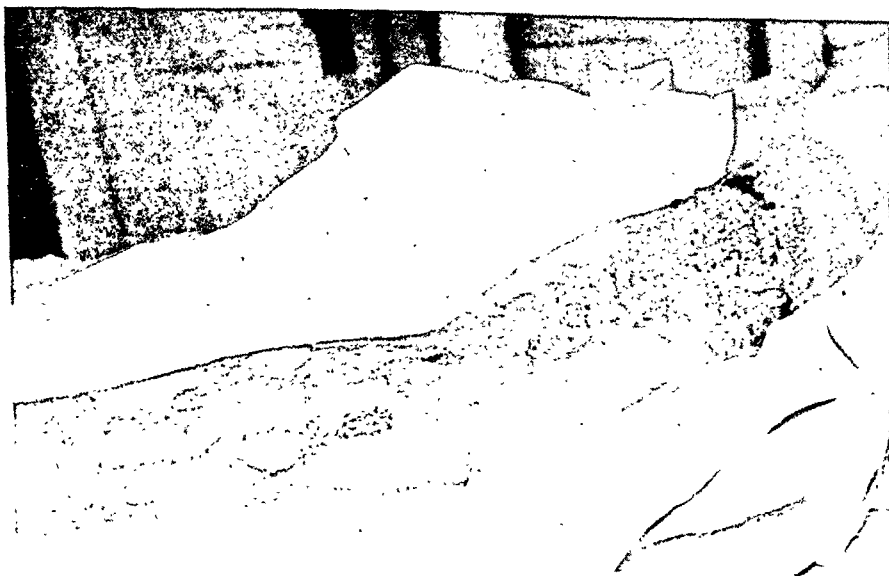


Fig. 3.—Left arm grafted with half-thickness Ollier-Thiersch grafts and kept soaked with the acetic acid-glycerin-normal saline solution for seven days postoperative. Continuous pressure was applied. There was approximately a 95 per cent take of the graft except at the top where the dressings slipped and dried out. Here the take was about 80 per cent.

# USE OF RECTUS SHEATH AND SUPERIOR PUBIC LIGAMENT IN DIRECT AND RECURRENT INGUINAL HERNIA

## PRELIMINARY REPORT\*

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**D**ESPITE improvements in surgical technique, recurrence rates for direct and recurrent inguinal hernia remain high. In a recent collection of end-result studies, covering a period of ten years, rates for direct inguinal hernia varied from 2.7 to 33.3 per cent, with an average of 15 to 20 per cent.<sup>21</sup> In 1934, Andrews and Bissell<sup>1</sup> reported a recurrence rate of 27 per cent and advocated abandonment of operation for direct inguinal hernia unless pain is present. Follow-up studies leave much to be desired and, hence, rates probably actually are higher than generally recorded. With competent surgeons, widely distributed, making such reports and expressing dissatisfaction with them, challenging scrutiny beyond technique and variations in basic method heretofore in general use is justified.

If it were possible to cover Hesselbach's triangle from the pubic spine with a layer of thick aponeurosis and anchor it to a solid structure by sewing clean fascia to clean fascia without tension, better results should be possible generally. This presupposes search for and elimination of peritoneal pockets at the internal ring.

Since late in 1943, I have employed procedures which seem to satisfy these postulates better than any now in general use. This rectus sheath-superior pubic ligament method is hitherto undescribed in the literature available. A boomerang-shaped flap of anterior rectus sheath is sutured to the superior pubic (Cooper's) ligament for a distance of 5 cm. from the pubic spine and the superior portion of the flap is sewed to the transversalis fascia up to the cord. The inguinal ligament is ignored. In addition, the cremaster envelope is opened at the internal ring and transversalis fascia is sewed to transversalis fascia as a collar about the actual structures of the cord. The external oblique fascia is sutured external to the cord.

Methods currently used for repair of direct inguinal hernia are essentially modifications of a technique described by Bassini<sup>7</sup> of Padua, Italy, about fifty-five years ago. The inguinal strata are sutured to the inguinal ligament. Bassini was comparatively unknown at that time, yet his work raised a historic surgical monument. In its day it rescued the surgery of hernia from despair and placed it on a firm foundation. Bassini's follow-up and results were good, even by today's standards. Of 251 cases, he followed all but four and 108 were followed from one to four and one-half years. He reported a 2.1 per cent recurrence rate. In contrast, the same year an English surgeon, known in America for his work on hernia, spoke before the Royal Medical and Chirurgical Society. Recurrence

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\*Presented at the meeting of the Wells County, Indiana, Medical Society, Nov. 26, 1944.

figures were given but omitted from publication. A discussant observed that in the vast majority of hernias in adults he believed the patient was relieved but not cured.

Surgery has come of age since 1890. Further advances have been made in anatomy. It has been possible to study structures in the inguinal region with greater care.<sup>3, 4, 15-18</sup> As a result, the very basis of the Bassini operation has been challenged, especially in the past few years. After a dissection of 300 inguinal regions, with the thought of continuity of aponeurosis and fascia in mind, McVay<sup>16</sup> described the inguinal ligament as essentially a guy rope. "The inguinal ligament," he wrote, "is not the site of insertion of either the transversus abdominis or internal oblique muscles, nor is it anchored securely enough to its fascial surroundings to serve as a substitute for this insertion." He stated that "pure fascia (for example, transversalis fascia) does not have the strength necessary to repair a musculo-aponeurotic defect such as occurs in direct inguinal hernias." He found that the "lowermost fibers of the internal oblique and transversus abdominis muscles do not attach to the inguinal ligament but insert into the fibrous covering of the pubic pecten, the ligamentum pubicum superius (ligament of Cooper)." According to his findings, the conjoined tendon usually is an artifact of dissection. In 7 per cent of dissections he found the lower transversus abdominis deficient.

#### SUPERIOR PUBIC LIGAMENT

The superior pubic ligament (BNA) was described in 1804 by Sir Astley Cooper (1768-1841). He is said to have advised its use in inguinal hernia operations.<sup>2</sup> Through the years it has received scant attention from anatomists and surgeons. It is accorded four lines of fine print "in the twenty-fourth edition of Gray's Anatomy, published in 1942."<sup>11</sup> It is a strong fibrous band, extending lateralward from the base of the lacunar ligament along the pectineal line of the superior pubic ramus, to which it is attached firmly. It is strengthened by the pectineal fascia and by a lateral expansion of the lower attachment of the linea alba called the adminiculum lineae albae. It can be felt in a hernia operation by retracting the cord and running the finger with pressure from the pubic spine medially and at an angle posteriorly as compared with the direction of the inguinal ligament. Lotheissen<sup>14</sup> reported using it in inguinal and femoral hernia in 1898. His first case was that of a 45-year-old woman who had been operated on for inguinal hernia twice before by the Bassini method. At the third procedure, in May, 1897, he was unable to perform the Bassini operation due to the destruction of the inguinal ligament and resorted to the use of Cooper's ligament. He quoted Narath of Utrecht as having performed the same procedure under similar circumstances. Subsequently, the method was used for femoral hernias by a number of authors in Europe and America. In 1927 Babcock<sup>5</sup> sutured the rectus sheath to the dense fibrous covering of the pubic pecten in inguinal hernia. In 1936 Dickson<sup>9</sup> suggested ignoring the inguinal ligament entirely. Impetus was given to interest in the subject by the anatomic studies of McVay and associates, previously referred to. Recently at Henry Ford Hospital in Detroit practically all hernia operations have been done by the superior pubic ligament technique.<sup>12</sup>

In November, 1943, Victor Satinsky and I applied the method as used by Harkins. To relieve tension we cut the rectus sheath as he did. Because of dissatisfaction with the relaxation thus produced and the inadequacy of the transversus abdominis in certain patients, we turned down a flap of rectus, a method which has been applied to the inguinal ligament.

#### THE RECTUS SHEATH

Bassini is said to have used the rectus sheath often in closures.<sup>2</sup> In 1892 Wolfer<sup>22</sup> cut the rectus sheath and used it in hernia repair. Slajmer<sup>20</sup> (1898) reported on 150 cases, using Wolfer's method. His drawing, however, shows an incomplete rectus flap sewed to the middle third of the inguinal ligament. The flap is not cut down to the pubis. Berger<sup>5</sup> (1902) and Halsted<sup>12</sup> (1903) turned down full flaps of rectus fascia in inguinal hernia repair. In 1941 Estes<sup>10</sup> reported 2.77 per cent recurrences in seventy-two direct inguinal hernias in which he employed the rectus flap to the inguinal ligament method.

The so-called conjoined tendon often is a very flimsy structure. McVay<sup>16</sup> found that it usually was an artifact of dissection. In 1940 Rienhoff<sup>19</sup> dissected 200 cadavers and found difficulty in demonstrating a conjoined tendon.

#### DESCRIPTION OF METHOD

If the incision ordinarily used for hernioplasty is placed 1 cm. superiorly and 1 cm. medially, exposure for the procedure to be described is improved. I have used a hockey stick type of incision. The external oblique aponeurosis is split over the cord, the cord and cremaster envelope separated from its bed, and the superior ramus of the pubis palpated as described previously.

The cremaster envelope is opened at the internal ring and the actual structures of the cord isolated. A peritoneal pouch has been looked for and found in each case. The pouch is opened, a finger inserted into the peritoneal cavity, the strength and redundancy of the floor of Hesselbach's triangle evaluated, and decision made as to the need for a rectus sheath-superior pubic ligament repair. In direct hernia the inferior epigastric vessels are isolated and direct and indirect sacs usually converted into one (Hoguet maneuver), ligated, and anchored high (Kocher). Then the transversalis fascia is sutured as a collar about the actual structures of the cord. Occasionally the transversalis here is flimsy, but not as often as earlier literature indicates. The cremaster envelope is closed.

Beginning at the pubic spine, the superior pubic ligament is exposed by blunt dissection, using the left index finger against the femoral vessels as a retractor. Oozing can be controlled with a small sponge pack. After approximately 6 cm. of ligament have been exposed, a flap is cut from the anterior sheaths of the rectus and pyramidalis muscles, as indicated in Fig. 1. Occasionally, a weak area will be found at the lateral edge of the rectus. A few sutures may be necessary. Ordinarily the rectus sheath is stout throughout, varying in thickness, of course, with the individual's general fascial endowments. Fine interrupted silk sutures are placed as indicated in Fig. 2, care being taken to include bundles of the rectus sheath fibers and touch bone along the superior ramus of the pubis. A small stout curved cutting needle is used.

Then transversalis fascia and the upper portion of the rectus sheath flap are sutured up to the cord with fine interrupted silk (Fig. 2). Tilting the table, feet down, at an angle of 45 degrees seems to facilitate the placing of sutures. The cord is allowed to fall into the resulting depression. The external oblique

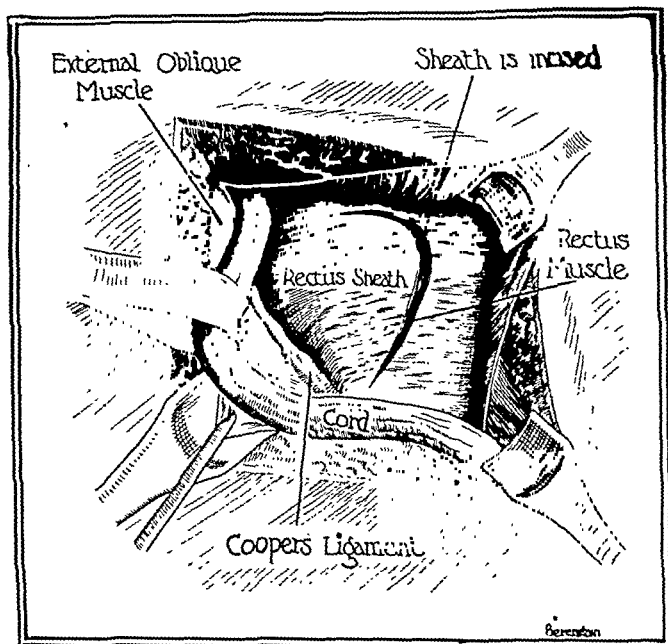


Fig. 1.—Illustrating incision in rectus sheath.

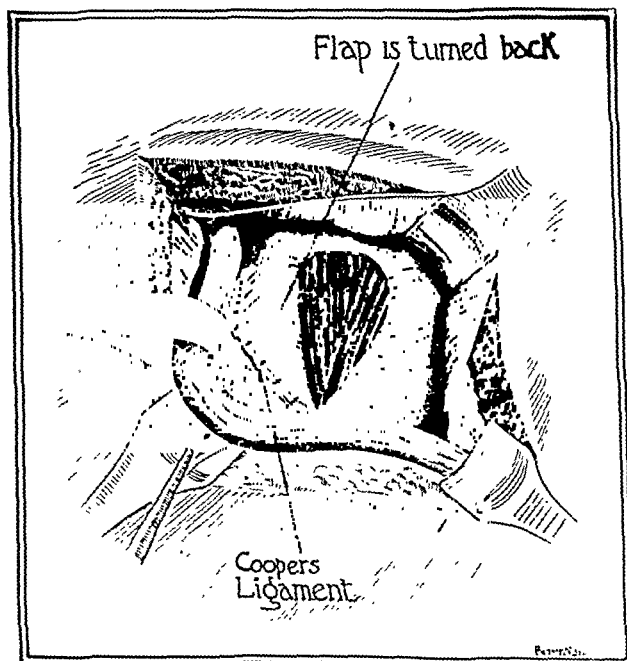


Fig. 2.—Illustrating suture of rectus sheath to superior pubic ligament.

aponeurosis and the superficial fascia then are sutured anterior to the cord. Nearly all patients were operated on by the silk technique. In a few of the early operations catgut was used. The reaction in silk sutured wounds has been minimal and no slough of sutures has taken place.

#### INDICATIONS

The method described seems indicated in (1) direct inguinal hernias, (2) indirect inguinal hernias where the fascia of Hesselbach's triangle, as shown by the palpating finger within the abdomen, is weak or greatly redundant, (3) recurrent inguinal hernias, and (4) femoral hernias.

#### IMMEDIATE RESULTS

Thirty-five patients have been operated on by one or both of the procedures outlined. The youngest patient was 19 years of age and the oldest 56. The average age was 25 years. In twenty-two direct inguinal hernias the rectus sheath-superior pubic ligament procedure was used and in eighteen of these the redundancy in the transversalis fascia collar around the actual structures of the cord was taken up. In thirteen the latter procedure alone was carried out. There were three recurrent hernias and in two of these the rectus sheath-superior pubic ligament procedure was used. There were no deaths. There was one instance of wound infection. All were checked after six weeks and no evidence of recurrence found.

#### DISCUSSION

The series reported here is too small and the follow-up too short to formulate any final conclusions. However, it is my impression from this experience that the operation is sound in principle and gives promise to lower recurrence rates in its field. Longer term follow-up studies are planned. It is well known that the most vulnerable area for recurrence is the lower angle where, in the Bassini operation, two fixed structures, the so-called conjoined tendon and the inguinal ligament are sutured. This cannot be done without tension, as emphasized by Stein and Casten.<sup>21</sup> In my opinion the procedure described harmonizes more with basic principles of plastic surgery. It permits suture without undue tension.

As pointed out by McVay,<sup>16</sup> the transversalis in this angle sometimes is developed poorly. Rectus aponeurosis meets this deficiency and in this respect seems to be an improvement over procedures involving the superior pubic ligament described heretofore.

It is interesting that on examination postoperatively with the finger in the external ring a different sensation is imparted than is found in more commonly performed herniotomies. Little or no transmission of impulse is felt.

The advantage of the procedure in recurrent hernia is that previously worked over scar-laden tissues are avoided and the operation is carried out in a virgin field. Recurrence rates therefore should approximate those of the primary operation.

The procedure requires more time to perform than the average herniotomy. As more experience is obtained, however, operating time discrepancy diminishes.

The sphincter action of the internal oblique at the internal ring is not disturbed. Any skeptic about such sphincter action should place his finger in the neck of an indirect hernial sac in a muscular patient who is allowed to recover partially from a general anesthetic.

Superior pubic ligament procedures safeguard against overlooking an occult femoral hernia and insure against subsequent development of femoral hernia.

Most of these procedures were done under spinal anesthesia, using mixtures of procaine and pontocaine.

#### SUMMARY

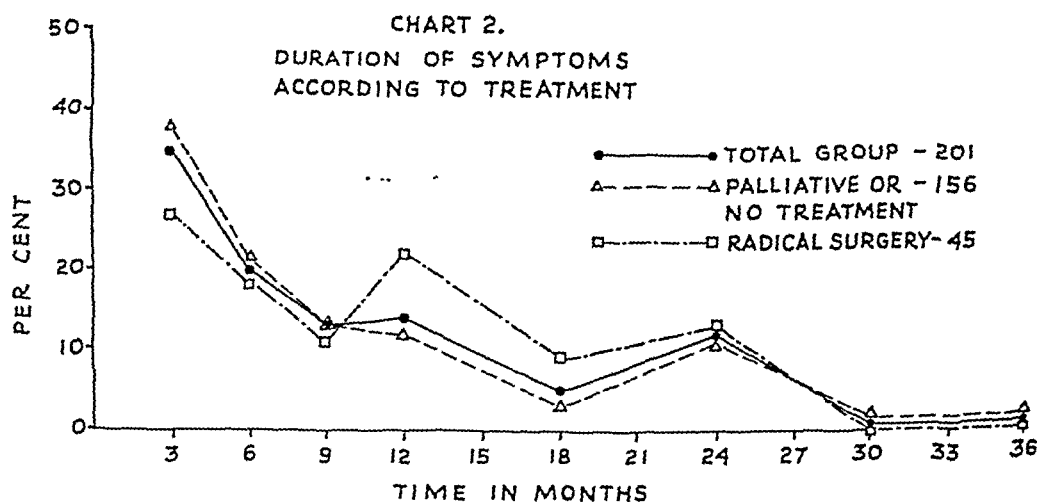
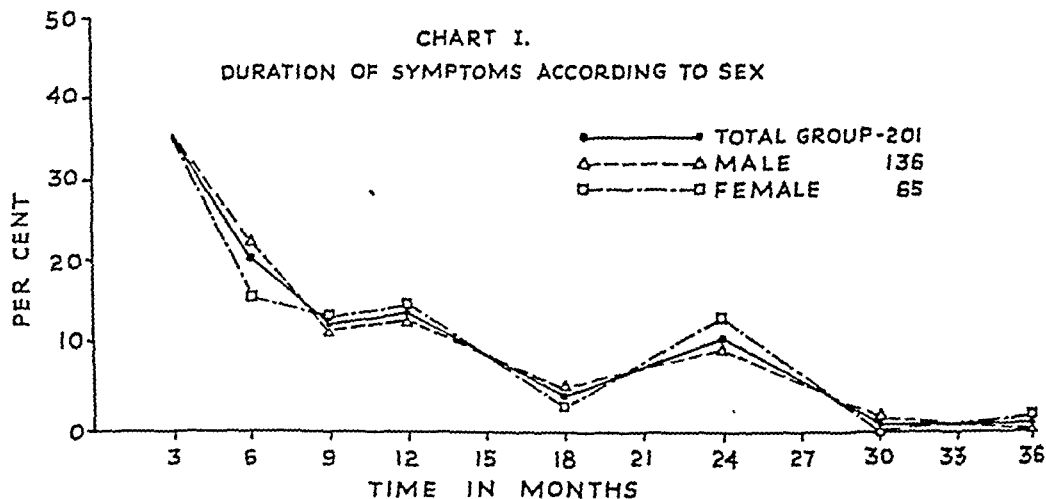
A method of hernioplasty is described wherein a flap of anterior rectus and pyramidalis sheath is turned down and sutured to the superior pubic ligament. Such a procedure is believed indicated in (1) direct inguinal hernias, (2) indirect inguinal hernias with weak and redundant fascia in Hesselbach's triangle, (3) recurrent inguinal hernias operated on previously by other methods, and (4) femoral hernias. Further work with the method and follow-up studies are planned.

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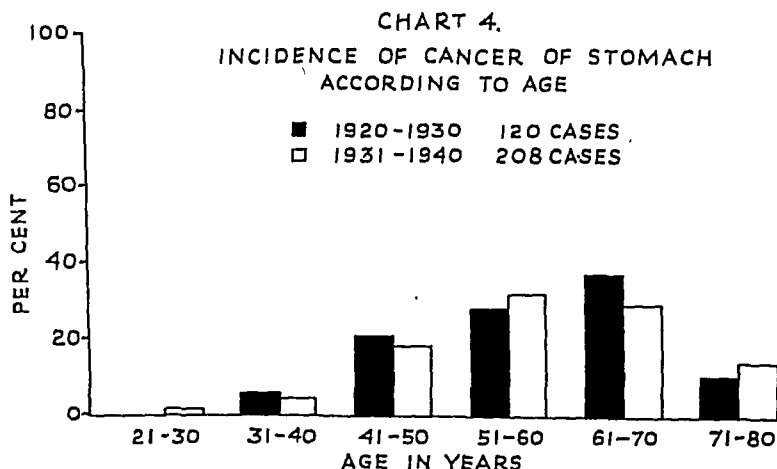
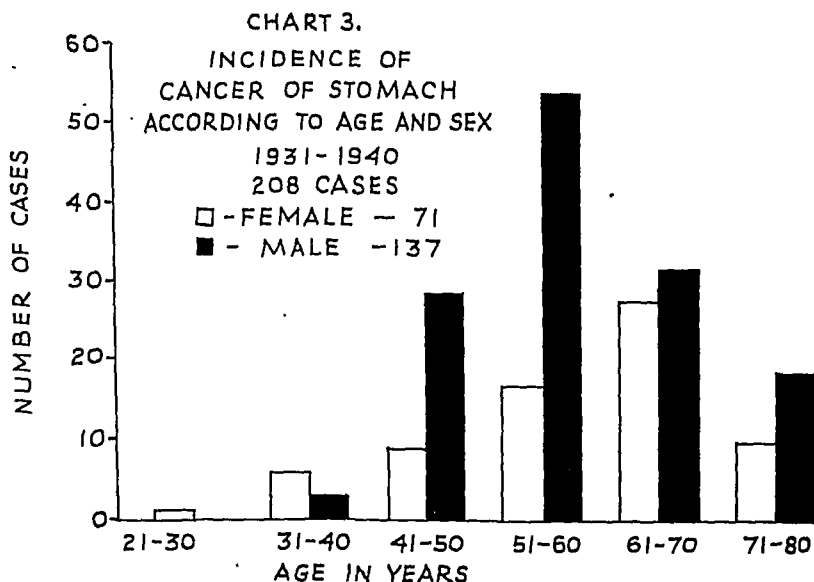


Of the total group of 201 patients whose histories were sufficiently reliable to establish the duration of symptoms, 136 were men and 65 were women. The curves of these two groups and the total group are essentially identical indicating that each sex was equally negligent in seeking treatment. The peaks at the twelfth and twenty-fourth months periods in Chart 1 are probably explained by the patient's inability to remember precisely the duration of their



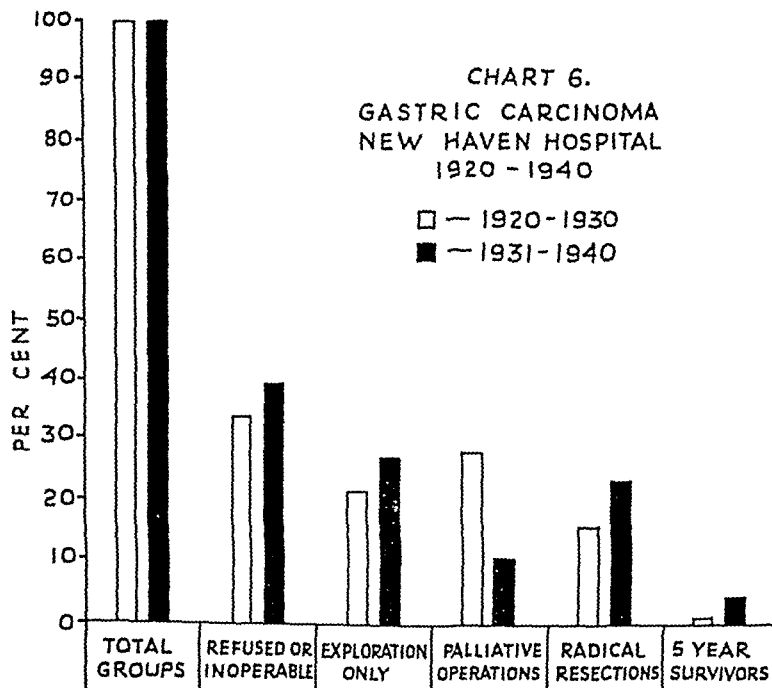
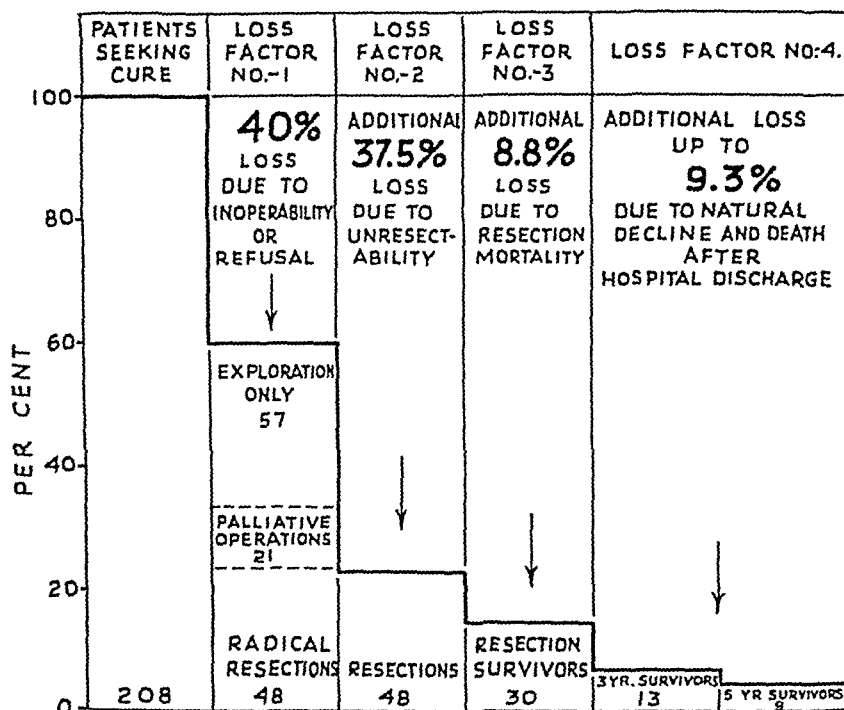
illnesses when they were of that length of time and a possible tendency of the history recorders to be negligent in seeking exact information when the symptoms were long drawn out. Chart 2 is interesting in that it reveals that many patients who were amenable to radical surgery had had symptoms for a long period. Thirty-eight per cent of the group who were nonresectable had had symptoms less than three months whereas in the radical surgery group, 27 per cent had had symptoms for a corresponding period of time. On the other hand, 22 per cent of the radical surgery group had had symptoms for nine months to one year compared with 12 per cent in the nonsurgical group.

Undoubtedly this indicates that many of the patients who had had symptoms for a long period were either harboring tumors of a low growth potential, had a high host resistance factor, or had a carcinoma arising in an ulcer. In any event, the relationship between the host and the tumor was such that the tumor could not or did not reach the inoperable stage in spite of its long residence in the host.

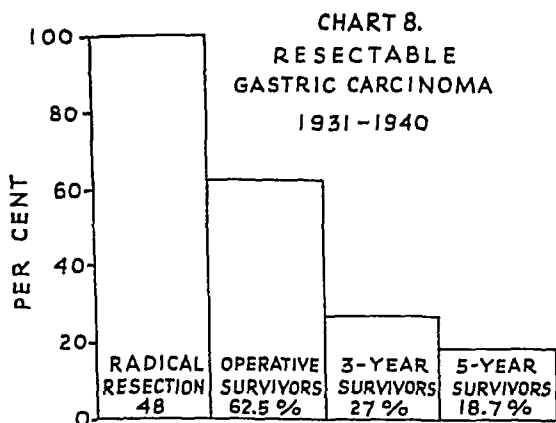
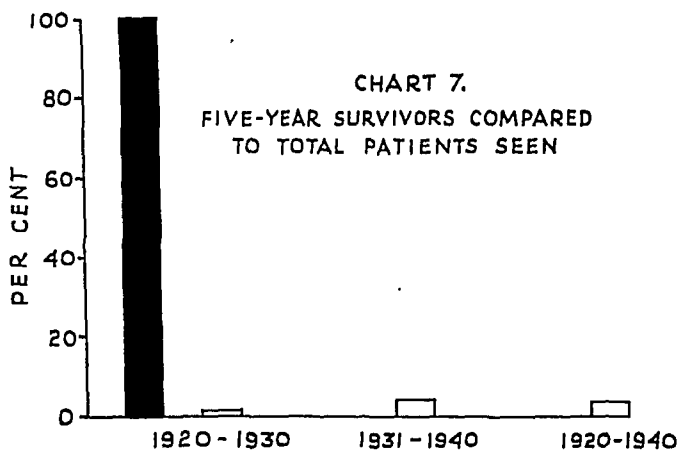


The preponderance of the disease in the male sex and in the sixth and seventh decades of life is well illustrated in Chart 3. It is interesting that the incidence of the disease is highest in men in the sixth decade whereas in women it is in the seventh. Chart 4 shows the comparative age distribution in the two periods. It would suggest that we are seeing disease in younger people than we did in the early decade, but probably the groups are so small that the difference is not of any statistical significance.

CHART 5.  
GASTRIC CARCINOMA - NEW HAVEN HOSPITAL 1931 - 1940



years, and it seems likely that they will, then 33 per cent of the operative survivors will be long-term survivors. The survival rate of resectable gastric cancer compares favorably with that of cancer of many other organs and is better than some, namely lung and hypopharynx.



A comparison of the operative mortality rates for the various types of procedures performed is shown in Table IV. There has been a fall in the gastrectomy mortality rate from 52.6 to 37.5 per cent. The latter figure is still much too high, but it is an improvement over the former. Perhaps it is only fair to state that it includes five total abdominal gastrectomies on patients who had extensive disease and were poor operative risks. On the other hand, their only chance for survival was through a gastrectomy and therefore the procedure was justified.

A study of the records of the patients who succumbed to the operation failed to reveal a significant single important cause for the deaths. Of almost equal prominence were peritonitis, with and without a perforated suture line, pneumonia, pulmonary embolism, coronary thrombosis, and unexplained reasons. Of some significance, however, is the fact that an occasional patient died

TABLE IV. OPERATIVE MORTALITY

OPERATION	NUMBER OF OPERATIONS		NUMBER OF DEATHS		MORTALITY (PER CENT)	
	1920-1930	1931-1940	1920-1930	1931-1940	1920-1930	1931-1940
Exploration	26	57	1	6	3.8	10.4
Palliation	34	21	11	6	32.3	28.5
Radical	19	48	10	18	52.6	37.5

from resection of what, during the course of the operation, proved to be a nonresectable tumor. The operator had already committed himself to a gastrectomy before this fact was ascertained. It is of the utmost importance to examine all of the critical points before committing one's self to the resection. The lesser peritoneal sack should be opened to make certain that the tumor has not invaded the retroperitoneal tissues, and the vicinity of the hepatic artery and common bile duct should be carefully inspected. The actual removal of the stomach should not be started until the surgeon is certain that he can do it without jeopardizing vital structures or cutting through tumor.

*Survivors.*—Four of the nine survivors were women and five were men. Three had regional lymph node involvement whereas six did not. Four gave past histories suggestive of an ulcer: one, nine years previously; a second, five years; a third, four years; and the fourth, three years. Four gave a present illness duration of one year. The others varied between one and ten months. Two of the nine died of carcinoma between five and six years after their resections had been done.

#### DISCUSSION

Cancer as a whole can be divided and classified into two large groups, the external or accessible, and the internal or inaccessible. In the former are such lesions as carcinoma of the skin, breast, mouth, and external genitals, including the cervix. They are characterized by the fact that they lend themselves to early detection either visually or by the examining finger. In the latter group are such malignancies as carcinoma of the lung, gastrointestinal tract, and kidneys. Lesions in these locations are not easily detected, particularly in their early stages, and may grow to a large size before causing symptoms that will lead a patient to see his physician.

In recent years considerable literature has appeared regarding the management of, and results obtained in, Cancer Prevention Clinics or, as they are sometimes called, Health Maintenance Clinics. Their purpose has essentially been one of periodic physical examination with the hope of detecting early external cancer and of preventing such cancer by eliminating chronic tissue abnormalities that might lead to cancer. Their scope, however, is being extended to internal cancer. St. John, Swenson, and Harvey<sup>3</sup> have reported 2,413 people on whom roentgenographic examination of the stomach was performed. The subjects were in the cancer age group, but all were without significant symptoms referable to the stomach. Three unsuspected tumors were found; two were carcinomas and one was a lymphosarcoma. At first glance this seems like a worth-while achievement. Three patients were sub-

mitted to treatment who might otherwise have been lost. However, one of these tumors could not be identified at the original operation, and it was only after the second abdominal exploration was carried out some months later that the tumor was definitely identified and resected. The magnitude of this approach to the detection of early gastric cancer is further emphasized by the fact that it would accordingly be necessary to do over 80,000 examinations to find 100 tumors. There is neither technical assistance available nor sufficient well-trained radiologists to organize and pursue a program extensive enough to make it worth while. Furthermore, one might raise the question whether even if there were sufficient help, the results achieved would justify the expense.

One must not lose sight of the fact that it is impossible for the clinician to make a diagnosis of early gastric cancer and that it is at times extremely difficult even for the radiologist to do so. Therefore, if this method is to be used for the early detection of gastric cancer, examinations must be repeated at least every six months throughout the cancer important decades. Such a task on a scale sufficiently broad and extensive to obtain significant results seems insurmountable at the present time. A single examination certainly will not suffice, nor, in view of the insidiousness of the onset of this disease, will yearly examinations be sufficiently frequent. Evidence for this latter point is the fact that 20 of the 208 patients in this series had had negative x-ray examinations of the stomach from six months to two years before the disease was finally detected.

*These paragraphs are not meant to discourage such cancer-detection programs. They represent a step in the proper direction in that they are attempts to find early and curable cancer. However, the magnitude of the task, particularly if projects large enough to be effective are started, the need for a far larger medical and technical personnel than is now available, and the expensive nature of the program should all be recognized. What seems to us to be a more realistic approach to the problem has been the work of Rigler, Kaplan, and Fink<sup>4</sup> on the relationship between pernicious anemia and tumors of the stomach. Roentgen studies of the stomach with barium were done on 211 patients with pernicious anemia. Eighty per cent had multiple examinations. Seventeen carcinomas and fifteen benign tumors were found. In other words, a disease which is known to predispose to cancer of the stomach was studied with a considerable degree of success.*

Of probably greater immediate importance is the ever-continuing propaganda with respect to the education of the public and physicians in early diagnosis and early treatment. The words, early diagnosis and early treatment, are in danger of becoming a trite phrase if they do not constitute one already. However, it is impossible to overemphasize the fact that a small early cancer is more favorable than a large late one. The educational literature of such organizations as the American Cancer Society seems to be slowly taking effect upon the public. Increasing numbers of patients appear for examination with symptoms that formerly might be considered insignificant.

pexis operation and both showed the early afferent arteriolar lesions associated with essential hypertension.

The technique of the operation was essentially the same as that reported<sup>10</sup> in the dog, which is as follows:

The kidney and the spleen were mobilized so they were easily apposed. A cruciate incision, about 1 cm. deep, was made in the kidney. The long axis ran over the convex surface from pole to pole. The shorter axis ran transversely at the midpoint of the longitudinal incision. The edges of this incision were undercut to give a flat raw surface. The spleen was incised from the free distal edge almost to the pedicle and undercut to give a flat surface the size of the cut kidney. The cut surfaces of spleen and kidney were then apposed and maintained in that position by means of three sutures of ribbon catgut. The catgut was brought through the substance of the kidney by means of a specially designed aneurysm needle to prevent its slipping off the rounded poles. It was then continued around the spleen between the vessels of the pedicle and the ends were fixed with a silk suture. The wide catgut was drawn tight enough to stop bleeding but not tight enough to cause pressure necrosis.

The results were uniform. In none of the three hypertensive patients was the blood pressure reduced for more than three weeks. The patient (L. A.) who had lowered blood pressure for three weeks was severely ill at the time with pulmonary embolism and infarction. The other two showed a fall in blood pressure only during the operation. After the operation the patients have been seen for one year, two years and ten months, and four years, respectively.

#### CASE HISTORIES

**CASE 1 (History No. 6329).**—L. A., aged 24 years, was a married Negro woman. Her first admission was on June 18, 1940. She was discharged Nov. 15, 1940.

The chief complaint was frequent headaches for fifteen years. Family history revealed that the mother and father were well, and the paternal grandmother had headaches and hypertension.

**Personal History.**—The patient was born in North Carolina and has lived in New York, N. Y., since 1935, working as a laundress. She has been married eight years and has two children, 8½ and 7 years old. One miscarriage was induced six years before. Prior to admission she lost twelve pounds.

**Past Health and Illness.**—Headaches, usually over the vertex of the skull, recurred for fifteen years. Relief was obtained with "B.C. powders," aspirin, walking about, and lately wearing glasses. The headaches were aggravated by menstruation, warm weather, smoking, alcohol, or eating pork or beef. They usually appeared late in the afternoon or evening. For several weeks the headaches were unilateral, involving the left side of the head, forehead, and neck. Six years before admission she developed attacks of exertional dyspnea and substernal aches which have increased in frequency and severity. Five years before she had a severe sore throat lasting one month. Three weeks after its onset the right foot swelled so that she could not wear a shoe. It required two months for the swelling of the foot to disappear. In March, 1940, at the Harlem Hospital, blood pressure and Wassermann test were normal. She returned to work but the headaches became worse. At the Metropolitan Hospital on June 18, 1940, blood pressure was 150/120; urine was normal. Red blood cell counts, serum nonprotein nitrogen, and proteins were normal. Electrocardiograms showed inversion of T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub> with left axis deviation. Diastolic pressure was usually over 100. She was transferred to the Research Division on Aug. 29, 1940.

*Physical Examination.*—Temperature was 98.6° F.; pulse, 90; respirations, 20; blood pressure, 138/94. The positive findings were as follows: (1) The patient was a well-developed, well-nourished, young woman who appeared well. (2) Slight narrowing of the arterioles of the eye grounds without exudation or hemorrhages was present. (3) The point of maximum impulse of the heart was 11 cm. to the left of the midline in the fifth intercostal space. The aortic second sound was accentuated. (4) The cervix was lacerated and the uterus was retroverted.

*Laboratory Data.*—Red blood cells were 4,530,000; hemoglobin, 91 per cent; white blood cells, 10,400; polymorphonuclears, 63 per cent; lymphocytes, 33 per cent; monocytes, 2 per cent; eosinophiles, 2 per cent. Blood: Glucose 77 mg. per cent; nonprotein nitrogen 27 mg. per cent; serum cholesterol 210 mg. per cent; serum albumin 4.8 per cent; globulin 2.9 per cent. Urine: Specific gravity 1.010 to 1.027; albumin 0; glucose 0. Addis counts: Red blood cells less than 1,000,000; white blood cells less than 1,000,000; casts less than 30,000; urea clearance 103 per cent of normal; phenolsulfonphthalein 80 to 90 per cent excretion in two hours. Mosenthal concentration test showed urine specific gravity 1.021 to 1.028; basal metabolic rate was -16 to -18; antistreptolysin titer ranged between 111 to 144 units. Kahn precipitation was 2+; roentgenogram of chest was normal; electrocardiogram showed T<sub>1</sub> inverted and small, T<sub>2</sub>, T<sub>3</sub>, and T<sub>4</sub> diaphasic. Retrograde pyelogram showed slight dilation of the right pelvis and calices but no calculi. The small degree of dilatation of the right pelvis was thought to be due to distention with the dye. Infusion with 1,500 c.c. of saline solution using the method of Caughey was followed by a maximum rise of 65 mm. of H<sub>2</sub>O above the initial venous pressure and by a 22 per cent fall in vital capacity. This was interpreted as indication of a decrease in cardiac reserve. By the cold pressor test, initial blood pressure was 150/110; after one minute of immersion of hand in cold water (4° C.) blood pressure was 200/160.

*Course.*—For two weeks the patient was treated with 30 mm. of saturated solution of potassium iodide because of a 2+ Kahn precipitation test. While in bed for one month she showed no improvement in blood pressure, which on thirty-one examinations ranged from 138/94 to 190/125. On Nov. 15, 1940, she was discharged to the Presbyterian Hospital where a splenorenopexy was performed, Dec. 2, 1940, by one of us (D. M. W.) and Dr. Allen O. Whipple. Blood pressure before the operation was 170/118; Kline test, 3+; Wassermann, 1+. The course was precarious for three and one-half weeks after the operation. On the eighth day there were signs of pulmonary embolism and infarction of the lower lobe of the left lung. During the stormy postoperative period of three and one-half weeks the blood pressure ranged between 100 to 110 systolic and 70 to 80 diastolic. For three days before discharge, which was five weeks after the operation, her blood pressure was recorded as 112 to 124 systolic and 90 to 92 diastolic. The patient was discharged from the Presbyterian Hospital on Jan. 6, 1941.

She was readmitted to the research division three times for further study. The first stay from Jan. 14 to March 23, 1941, followed her transfer from the Presbyterian Hospital. On the day of admission the blood pressure was 150/106. During her stay of ten weeks the blood pressure did not vary significantly from this level. In spite of the persistent hypertension, the headaches had diminished in frequency. There were no significant cardiac or urinary changes. On Feb. 17, 1941, an intravenous pyelogram showed no abnormal changes. Four days later the patient developed the signs of catarrhal jaundice which cleared after three weeks. The blood pressure did not fall during the period of jaundice.

Her second readmission was from Nov. 10 to 17, 1941, for the termination of a five and one-half month pregnancy. The operation was subsequently performed at Welfare Hospital. Blood pressure was 156/116 at this time. In the nine-month interval between this and the previous stay in the hospital, blood pressure ranged from 165 to 185 systolic and 110 to 120 diastolic. The urine contained  $\pm$  albumin without cellular elements. Hysterectomy was followed by no significant changes in blood pressure. During the operation the spleen and left kidney were found to be firmly adherent to each other. Both organs were soft and appeared viable. Phenolsulfonphthalein test on Nov. 17, 1941, showed 95 per cent excretion in two hours. Kahn precipitation test was negative.



The third readmission was from March 16 to April 2, 1942. For three months before she had had nocturia three to four times nightly and intractable headaches. Bed rest was associated with disappearance of the headache. Urine function tests were normal according to phenolsulfonphthalein excretion of 90 per cent in two hours; urine specific gravity was 1.028; albumin, 0; red and white blood cells and casts negative; urea clearance was 77 per cent of normal and blood urea nitrogen, 87 mg. per cent. Blood pressure range was 150 to 180 systolic and 100 to 110 diastolic.

This patient was last seen on Nov. 30, 1944, approximately four years after the operation, when her blood pressure was 190/130. Headaches and exertional dyspnea were the dominant symptoms. Examination of the urine revealed 3+ albumin, two to three red blood cells per high power field, and a rare granular cast. The blood count, sedimentation rate, and nonprotein nitrogen were normal.

*Biopsy Specimens.*—There was no specimen of renal tissue. However, the tissues of the uterus and of all the organs of the fetus, which included heart, aorta, lungs, spleen, liver, pancreas and gall bladder, adrenals, thyroid, testes, brain, pituitary, thymus, and spinal cord showed no vascular alterations.

In summary, splenorenopexy was performed on a woman of 24 years with about nine months of observed hypertension. Renal function tests were within the normal range. For three weeks after the operation the blood pressure was within the normal range but this period was associated with pulmonary embolism and infarction, hemothorax, and pneumonia. Thereafter, the blood pressure returned to the preoperative level. In the past two of the four postoperative years the level of the blood pressure has gradually risen beyond that of the preoperative period.

**CASE 2 (History No. 2704)**—E. E., a 30 year old married man, was a white American, metal worker. He was admitted March 10, 1941, and discharged March 14, 1941. His chief complaint was palpitation and sense of suffocation for two years. Family history revealed that the patient's mother died of pulmonary tuberculosis at the age of 31 years. Father and sister were well.

*Personal History.*—The patient was born in New York, N. Y. and has always lived there. He has been married eight years. He drinks six cups of coffee daily and takes "nerve" pills. In addition, the patient has consumed fairly large amounts of alcohol for the past five years.

*Past Health and Illness.*—He has three to four colds a year. He had scarlet fever at 9 years of age, without sequelae. Sinusitis with headaches was present for several years.

*Illness at Time of Admission.*—For three or four years he had been "nervous." This was aggravated by the loss of his job. Episodes of palpitation and suffocation were noted about one and one half years before and in May, 1940, he was told by a doctor that he had an elevated blood pressure. For about two years he had spots before his eyes, blurred vision, and an inability to read print. At Manhattan Eye and Ear Hospital he was told that he had optic neuritis.

*Physical Examination.*—Temperature was 99.6° F.; pulse, 92; blood pressure, 170/120. The positive findings were as follows: (1) The patient was a well developed but poorly nourished, young adult man, who did not appear ill. (2) The eye grounds revealed poorly defined, hazy discs indicating optic atrophy. (3) The arterioles appeared normal. No exudate or hemorrhages were visible. (4) Many teeth were missing. (5) The heart was overactive, but not enlarged. The aortic second sound was accentuated.

*Laboratory Findings.*—Roentgenogram of the chest showed a normal cardiac shadow. Red blood cells were 4,940,000, hemoglobin 99 per cent, white blood cells 13,000, polymorpho nuclears 65 per cent, lymphocytes 26 per cent, monocytes 6 per cent, basophiles 1 per cent, and eosinophiles 2 per cent. Blood glucose was 102 mg per cent, creatinine 1.2 mg., urea nitrogen 12 mg. per cent, cholesterol 250 mg per cent, serum albumin 4.8 Gm. per cent, globulin 2.5 Gm. per cent, nonprotein nitrogen 26 mg per cent. Urine: Specific gravity was 1.002 to 1.020, albumin 0 to  $\pm$ , glucose 0, Addis counts. Red blood cells less than 1,000,000, white blood cells less than 1,000,000, casts less than 30,000. Blood Wassermann was negative.

*Course.*—The second admission was March 20 to May 24, 1941. Blood pressure during the following nine weeks of bed rest varied between 135 to 170 systolic and 95 to 110 diastolic. Phenolsulfonphthalein excretion was 85 per cent in two hours. Urea clearance was 101 per cent of normal. Electrocardiogram on March 24, 1941, showed a well-marked left ventricular preponderance. Retrograde pyelogram, April 2, 1941, showed normal renal pelvises. There was acute angulation between the right pelvis and ureter. This procedure, repeated on May 14, 1941, revealed a normal right renal tract. Cold pressor test before the operation showed the blood pressure increase from a base of 150/100 to 200/130 in one minute. The patient was transferred to the Presbyterian Hospital where a splenorenopexy was performed by one of us (D.M.W.) and Dr. Whipple. Pneumonia developed on the fourth postoperative day and the wound was disrupted. This was closed under local anesthesia, and the fever and cough subsided with the administration of sulfadiazine. He was discharged from the Presbyterian Hospital on the twenty-ninth postoperative day.

The third admission followed his discharge from the Presbyterian Hospital and lasted only one day, from June 24 to June 25, 1941. Blood pressure was 145/100.

The fourth admission was Oct. 3 to Oct. 15, 1941. Blood pressure was 146/96. The urine showed a specific gravity of 1.017, albumin  $\pm$ , and no cells or casts in the sediment. After a week he was discharged to return for the fifth admission on Oct. 29, 1941, when he left the same day. The sixth admission was April 15 to May 21, 1942. There was a minimal ankle edema for about one week before admission, along with exertional dyspnea. After one day of bed rest the edema disappeared. April 16, 1942, serum nonprotein nitrogen was 28 mg. per cent, cholesterol 196, serum albumin 4.4 Gm. per cent, globulin 1.4 Gm. per cent, phenolsulfonphthalein 80 per cent excretion in two hours, urea clearance 64 per cent of normal, urine albumin  $\pm$ , with no cellular elements in the sediment.

He has been seen on eleven occasions since his discharge, the latest examination having been on April 15, 1944. His pressure ranges between 140 to 170 systolic and 96 to 116 diastolic. He is working again and his symptoms are similar to those experienced before the operation.

*Biopsy Specimens.*—May 26, 1941, the arterioles of the spleen and kidney showed intimal thickening due to the presence of an acidophilic hyaline material. There were no proliferative lesions in the glomeruli, or changes in the basement membranes of the tufts. The tubules and interstitial tissue as well as the medium-sized arteries were unaltered.

In summary, a splenorenopexy was performed on a 30-year-old man who had had the signs and symptoms of essential hypertension for about two years. The renal changes as observed in the biopsy were consistent with this diagnosis. There was no lowering of the blood pressure for two years and ten months after the pexis was made. For a short time there was some relief from his presenting symptoms of palpitation and dyspnea.

**CASE 3 (History No. 129808).**—E. K. was a white, American, housewife, aged 32 years. She was admitted March 12, 1941, and discharged July 15, 1941.

Her chief complaints were daily headaches and a known high blood pressure for five months. Family history revealed that her mother had died at 42 years of age following a gall bladder operation; her father was killed in an accident; one sister had high blood pressure, two sisters and three brothers were well.

*Personal History.*—She has always lived in New York, N. Y. Her husband, to whom she has been married sixteen years, was well. Miscarriages occurred at one, two, and five months, respectively, and she has no children. She gained seventy pounds during the two years before admission; upon entering the hospital her weight was 203 pounds.

*Past Health and Illness.*—She has colds two to three times a year. Scarlet fever occurred at the age of 7 years, without sequelae, diphtheria at the age of 14, erysipelas at the age of 11. Various operations of the following nature were performed: tonsillectomy at the age of 12 years, appendectomy at the age of 17, removal of Fallopian tubes at the age of 18, hysterectomy for fibroid at the age of 25, drainage of left ear abscess at the age of 26, hernia repair at the age of 27, repeat tonsillectomy at the age of 30.

*Illness at the Time of Admission.*—For twelve years she had had occipital headaches occurring every two to three weeks. Nervousness had been present for five years. Ankle edema lasting two weeks occurred in 1936 and disappeared after one week of thyroid administration. Orthopnea of two years' duration has required two pillows for comfort. Severe dyspnea from climbing one-half flight of stairs has been more severe with a recent gain of sixty-seven pounds. In 1938 the blood pressure range was said to be 118 to 210 systolic and 70 to 78 diastolic. In 1939, it was observed at 184/128. Blurred vision was present for six months. Glasses improved her vision. During the last five months she had six epistaxes. Five months before admission there was a sudden severe pain in the right eye associated with ecchymosis of the right conjunctiva. Blood pressure at that time was 230/170.

*Physical Examination.*—Temperature was 98.8° F.; pulse, 83; respiration, 20; blood pressure 236/152. The positive findings were as follows: (1) The patient was a very obese woman who was in no distress. (2) There was an increased amount of hair present on the chin, upper lip, forearms, and legs. (3) The eye grounds revealed arterial narrowing with the "silver wire" light reflex, and small deposits of dark brown pigment immediately lateral to both optic discs. (4) The heart was not enlarged. There were midline and right lower quadrant postoperative scars. The question of Cushing's syndrome was raised, but could not be substantiated.

*Laboratory Findings.*—Red blood cells were 5,600,000, hemoglobin 114 per cent, white blood cells 13,000, polymorphonuclears 63 per cent, lymphocytes 24 per cent, monocytes 10 per cent, basophiles 1 per cent, eosinophiles 2 per cent. Urine: Specific gravity was 1.010 to 1.026; albumin, 0 to  $\pm$ ; sugar, 0; rare red and white blood cells, Addis counts: Red blood cells usually less than 1,000,000, white blood cells less than 1,000,000, casts less than 30,000. Blood glucose 95 mgm. per cent, urea nitrogen 15.5 mg. per cent, cholesterol 292 mg., serum albumin 4.8 Gm. per cent, globulin 2.3 Gm., phenol-sulfonphthalein excretion 90 per cent in two hours, basal metabolic rate +1, serum calcium 9.7 mg. per cent, phosphorus 3.8 mg. per cent, phosphatase 3.6 Bodansky units, urea clearance 106 per cent of normal. Electrocardiogram: Diphasic T in Lead I with moderate slurring of QRS complex in the first three leads. Roentgenograms of skull and sella turcica, chest, and abdomen were normal. Retrograde pyelogram was normal.

*Course.*—On a diet of 900 to 1,200 calories daily the patient's weight declined to 165 pounds during her stay of seventeen weeks in the hospital. Blood pressure varied from 145 to 220 systolic and from 90 to 165 diastolic during the stay. The headaches appeared to be improved by the administration of benzedrine in 5 mg. doses. The injection of typhoid vaccine intravenously had no influence on the blood pressure although it elevated the temperature to a maximum of 103° F. for three days. She was discharged to the Roosevelt Hospital, which she entered Sept. 19, 1941. A splenorenopexy was performed by one of us (D. M. W.) on Nov. 27, 1941. Although the blood pressure fell to 130/80 a few hours after the operation, it returned to 170/104 the next day. The temperature rose to 104.2° F. on the third day and returned to normal after twelve days. Blood pressure during the next three months varied from 140 to 190 systolic and 90 to 120 diastolic. There were no significant changes in the urine sediment. Since operation the headaches have not been reduced. Blood pressure on Sept. 4, 1942, was 240/150. There was no follow up.

*Biopsy Specimens.*—Biopsy of the kidney showed intimal thickening of some of the afferent glomerular arterioles with a pink-staining hyaline substance. An occasional glomerulus had hyaline thickening of a portion of a loop. No adhesions, or crescent or epithelial proliferations were seen in the glomerular tufts. The convoluted tubules contained a granular precipitate although the lining epithelial cells were unaltered. The spleen showed hyaline thickening of the intima of the arterioles. The medium-sized arteries were unaltered.

In summary, the patient was a woman of 32 years, with a history of many operations. Hypertension was discovered about one year before splenorenopexy. Biopsy of the kidney was characteristic of early arteriolar sclerosis. For one year following splenorenopexy there was no decrease in blood pressure or relief from other symptoms.

## DISCUSSION

There have been reports of unsuccessful attempts to lower the blood pressure of patients with hypertension by fusing the omentum and kidney.<sup>3</sup> In the dog, omentorenopexy was also without permanent effect on the hypertension following renal ischemia resulting from bilateral constriction of the renal arteries.<sup>8</sup> The temporary effect of omentorenopexy on the hypertension of dogs with renal ischemia contrasts with the permanent effect of splenorenopexy which lowers the blood pressure in such hypertensive dogs. The difference observed between the two operations in dogs is probably due to the greater collateral circulation produced by splenorenopexy than by omentorenopexy, since the tissue of the spleen is much more vascular than that of the omentum.

There is good evidence of "essential" hypertension in two of the three patients on whom the splenorenopexy was performed. This evidence rests not *only on the clinical and laboratory data but also on the characteristic arteriolar thickening of the kidney vessels observed in the biopsies.* Failure to lower the hypertension by splenorenopexy in these patients suggests several possible explanations, none of which can be proved at present. The pexis may not have produced a collateral circulation between the spleen and kidney. However, the operation in man was identical with that performed in the dog. The amount of renal and splenic parenchyma apposed by the operation in man was comparable to that in the dog. Whether a collateral circulation between the spleen and kidney was functioning in these patients can be proved only by removal and examination of the fused organs.

## CONCLUSION

Splenorenopexy which had resulted in a lowering of the blood pressure to normal in hypertensive dogs with bilateral constriction of the renal arteries had no significant effect on the blood pressure of three patients with "essential" hypertension.

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to the upper portion of the right kidney. Quite a number of arteries and veins of wider and smaller caliber were proceeding to this growth which, no doubt, belonged to the adrenal. The vessels were carefully ligated without any considerable hemorrhage occurring. While the tumor was easily detached from the kidney, its upper pole presented a few stronger adhesions to the diaphragm which had to be dissected off partly by sharp, partly by blunt, instruments.

On the whole, the tumor was sharply outlined and could be removed in toto in its capsule. All layers were then closed and a rubber drain introduced and left in place for twenty-four hours.

At the beginning of the operation the blood pressure was 140/90. Manipulations on the tumor in situ caused an increase in the systolic blood pressure to 300. Immediately after the operation it dropped to 105. After intravenous injection of  $\frac{1}{8}$  mg. of epinephrine, the systolic blood pressure rose again to 300. This rise, however, lasted but a few minutes and was followed by another drop to 65/0, the patient now being in a state of shock. During the following two days, an intravenous drip of saline solution containing 6 mg. adrenalin in all was given, in addition to intramuscular injections of adrenal cortex extract (supracort 9 c.c.). After three to four hours, the blood pressure increased to 105/75 and could be maintained at that level.



Fig. 1.

*Pathologic Examination of the Tumor.*—The specimen was a round tissue mass weighing 95 Gm. and measuring 6 by 5.5 by 4 cm. in diameter (Fig. 1). The mass was of a rubberlike consistency. Cut surfaces showed a moist tissue which was of a greyish-brown or cyanotic-reddish color. Underneath the fibrous capsule there were several islets of brightly yellowish cortical tissue.

*Microscopy.*—Sections from the central mass of the tumor were composed of epithelium-like cells, approximately the size of liver cells. They formed solid nests within a stroma consisting almost entirely of discrete fibrous septa or narrow blood capillaries (Fig. 2). In some areas the capillaries displayed sinusoid dilatation which sometimes occupied a larger portion of the tissue than the cellular component. Adjacent to wider capillaries the tumor cells were elongated and presented a radial arrangement converging toward the capillary lumen. The nuclei were clear, vesicular, and surrounded by a dark nuclear membrane. Rarely, single giant nuclei were seen or larger cells containing two to six nuclei of the described type. On staining, the cytoplasm was moderately eosinophilic. After fixa-

tion in Orth's solution, a distinct chromaffin reaction was noted in the cytoplasm of the tumor cells as well as in the sparse fibrous stroma which stained diffusely brown or contained scattered brown droplets.

All over the tumor ganglionic cells were scattered, isolated, or in groups of two or three.

*Anatomic Diagnosis.*—Pheochromocytoma of suprarenal medulla.

*Chemical Examination.*—Immediately after extirpation, a specimen of the tumor was submitted for chemical determination of the adrenaline content.\*

By the colorimetric method (Ewin's test in buffered solution) approximately 2 mg of adrenaline per gram of tissue were determined, corresponding to approximately 190 mg of adrenaline for the tumor as a whole.†

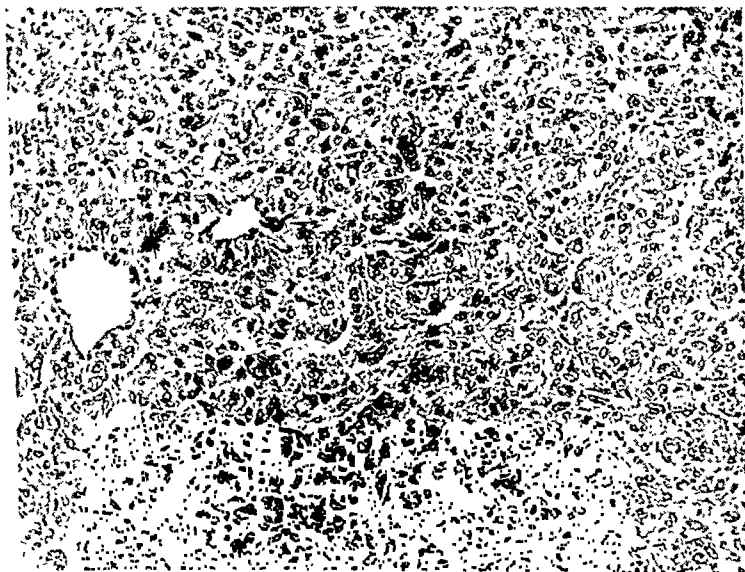


Fig. 2.

After his discharge from the hospital the patient was examined at frequent intervals up to the date of the writing of this report (July 12, 1945). Clinical, ophthalmoscopic, and laboratory findings during that seven months' period were as following: The patient's general condition improved markedly, his appetite was better, he gained in weight, and felt physically fitter. Not a single paroxysm of the type described had occurred since the operation. Tachycardia and perspiration disappeared. The blood pressure, taken on many occasions, varied between 130/90 and 120/85. The gallop rhythm as well as the systolic murmur had disappeared.

The electrocardiogram which, prior to the operation, had shown diphasic T waves in all leads with lowered S-T, and S-T<sub>2</sub> showed (on July 12, 1945) the same pattern in Lead II while in Lead II S-T was only slightly lowered. In Lead III, S-T was isoelectric and there was a positive T wave.

The x-ray of the heart which, prior to the operation, had shown enlargement especially to the left, with associated enlargement of the great blood vessels, did not show any appreciable change after the operation.

\*The chemical examination was performed by Dr. G. Brueckmann of the Section Pharmacology, Department of Applied Physiology, Hebrew University.

†The normal adrenaline content per gram of adrenal medulla (wet) is given as about 0.4 mg. (Belt and Powell<sup>6</sup>). Values up to 20 mg. of adrenaline per gram of tumor tissue have also been reported.

*Eye Fundus.*—As early as ten days after the operation, papilledema showed signs of regression and the large retinal hemorrhage began to be absorbed. This improvement continued and, on February 18, almost complete absorption had taken place. There was no change in the vascular findings. On May 13, papilledema had practically disappeared and there was no longer any evidence of hemorrhage in the retina. The blood vessels showed no improvement and the degenerative patches remained unchanged. The same findings were obtained on July 10, 1945.

*Laboratory Findings.*—Glycosuria and hyperglycemia disappeared completely in the course of time, after the highest blood sugar level recorded during paroxysm prior to the operation had been 304 mg. per cent, while between attacks it had dropped to as low as 66 mg. per cent. After the operation, the fasting blood sugar level was within normal limits. The blood sugar tolerance curve also showed normal values (February 25). The cholesterol content of the serum which, prior to operation, had amounted to 400 mg. per cent gradually came down to reach a level of 253 mg. per cent on May 16 and 220 mg. per cent on July 12. Albuminuria which, before the operation, had been of a marked degree, disappeared completely. The maximum specific gravity rose from 1023 before operation to 1028 on July 12. The urea clearance test which, prior to the operation, had been indicative of a reduced kidney function (47 per cent) now, 6 months after operation, yielded normal values (72 per cent, standard clearance).

#### COMMENT

The characteristic clinical manifestations of pheochromocytoma are paroxysms of hypertension accompanied by headache, palpitations, perspiration, nausea, and occasional vomiting. These paroxysms, as a rule, occur in the morning usually after the patient has washed or shaved. In exceptional cases, the vascular changes may lead to persistent hypertension (Thorn and Hindel<sup>7</sup>) with severe involvement of the eyes, the heart, the brain, and kidneys, and the clinical syndrome of malignant hypertension may develop (Kremer<sup>8</sup> and our own case). Some of the cases present paroxysmal hyperglycemia and glycosuria (Labbé and associates<sup>4</sup>). In our patient the hyperglycemia and glycosuria which were present showed no parallelism to the height of the blood pressure.

The diagnosis of pheochromocytoma can be verified by x-rays. Intravenous and retrograde pyelograms may show displacement of the kidney and distortion of the kidney pelvis and calices. If the tumor is small it can only be visualized by perirenal insufflation (Cahill<sup>9</sup>), a procedure that is, however, occasionally followed by undesirable side-effects and, therefore, dangerous (MacCullagh and Engel<sup>10</sup>). In a review of the cases of pheochromocytoma published in the literature by Biskind, Meyer, and Beadner<sup>11</sup> the results of the visualization methods are summarized in Table I.

In our case, the plain picture and pyelograms revealed no abnormal findings. Although tomography was tried, owing to lack of experience with this

TABLE I

	NUMBER OF CASES	
	POSITIVE RESULTS	NEGATIVE RESULTS
Plain picture	3	6
Intravenous pyelography	4	7
Retrograde pyelography	9	4
Perirenal insufflation	4	1

new method, the tumor could not be visualized and exploratory operation had to be resorted to. A careful study of the films *after* the operation quite clearly disclosed the presence of a round shadow above the right kidney (see Fig. 3), showing the tomogram focused at a distance of 13 cm. from the back. (Note the round shadow in the right paravertebral subdiaphragmatic region.)

From this experience it appears that the method may prove the surest and safest means of diagnosing a suprarenal tumor and should, therefore, be employed in similar cases.

Among other diagnostic measures, manual pressure on the region of the kidney may be tried, pressure on the affected side being likely to produce a typical paroxysm of hypertension (MacKenzie and McEachern<sup>12</sup>).

Pharmacologic tests have also been devised as a means to diagnose a pheochromocytoma. Beer, King, and Prinzmetal<sup>13</sup> made determinations of the adrenaline level of the blood by perfusing a rabbit's ear and Strombeck and Hedberg<sup>14</sup> did the same by chemical methods. Although they reported hyperadrenalinemia for their cases, the results are likely to be inconstant (Biskind



Fig. 3.

and associates<sup>11</sup>) and the procedure is not simple. Recently, a new test method has been described by Roth and Kvale,<sup>15</sup> consisting in the intravenous injection of 0.05 mg. of histamine which induces typical paroxysms of hypertension in patients with pheochromocytoma. The method is based on the fact that the denervated cat's pupil is dilated by histamine only in the presence of the adrenal glands. It is assumed that the injection of histamine causes an outpouring of adrenaline from the adrenal medulla (Kellaway and Cowell, quoted by Roth and Kvale<sup>15</sup>). An excessively high potassium level in the serum of patients suffering from pheochromocytoma has been ascertained by MacQuarrie (quoted by MacKeith and MacKeith<sup>16</sup>). Where all these methods fail to verify the diagnosis of pheochromocytoma, the clinical symptomatology alone may be considered sufficient reason to justify an exploratory operation. In the case re-



ported by Bauer and Leriche,<sup>17</sup> similarly to our own, the patient was first operated upon on the wrong side. In cases reported upon by Binger and Craig,<sup>15</sup> MacKenzie and McEachern,<sup>12</sup> and MacKeith and MacKeith<sup>16</sup> the tumor was also located by exploratory operation only, and successfully removed.

Where conditions are unclear, as in the case referred to, Young's method may be recommended, which enables exploration of the suprarenal regions on both sides from one and the same incision.

The removal of the tumor is attended with the risk of two serious complications. First, during the manipulations on the tumor, an excessive rise of the blood pressure may occur (Strombeck and Hedberg<sup>11</sup> and our own case) which is only forestalled by operating very carefully, without tearing of the capsule, and by dissecting the tumor as rapidly as possible. The second and far more dangerous risk attending the operation is a sudden and excessive drop of the blood pressure and shock after removal of the tumor. According to Biskind and his co-workers<sup>11</sup> shock occurred during or after the operation in eighteen out of a total of twenty-nine cases of pheochromocytoma (very severe in fifteen and only slight in three). In practically all cases in which death occurred during or after the operation it was apparently a result of shock due to a sudden decrease on the adrenaline level of the blood. The treatment, devised by Pinkoffs and Shipley<sup>5</sup> for this shock during or after operation consists of administration of epinephrine. It may be given in an intravenous drip of saline solution. The dose and the length of time during which administrations should be continued depends on the level of the blood pressure.

It has been pointed out (MacKenzie and McEachern<sup>12</sup>) that the effect of epinephrine may wear off with continuation of the treatment. Strombeck and Hedberg,<sup>14</sup> Van Epps, Hyndman, and Greene,<sup>20</sup> and MacKeith<sup>16</sup> gave cortical hormone preparations and salt solutions with good effect. Preoperative treatment with salt and cortical hormone has also been recommended (Biskind and associates<sup>11</sup>).

In our case, epinephrine was given as an addition to an intravenous drip of saline solution for one and one-half days following the operation, the amount administered totaling 6 mg., in addition to 9 c.c. of supracort. The blood pressure which, immediately after the operation had come down to the excessively low level of 65/0, was by this therapy kept within normal limits (105/75).

#### RESULTS

The results of this operation are reviewed by Biskind and his co-workers.<sup>11</sup> Including the case observed by these authors, twenty-nine patients had been operated upon up to 1940. Eight more cases were added to this list by MacKeith,<sup>16</sup> including one of his own. Since then, seven additional cases have been reported upon (MacCullagh and Engel,<sup>10</sup> Thorn and Hindel,<sup>7</sup> Hyman and Mencher,<sup>21</sup> Tennenbaum,<sup>22</sup> and Kenyon<sup>23</sup>) so that the operation was performed on a total of forty-five patients with pheochromocytoma (including the one referred to previously). Of these, ten died during or immediately after the operation. The progress in operative technique as well as in the management

of the postoperative phase after operation for pheochromocytoma is seen from the fact that until the end of 1936, seven deaths occurred among nineteen operations, whereas of the twenty-one patients operated upon after 1936 no more than three died. After successful operation, recovery is usually complete.

Malignant pheochromocytoma with associated hypertension is rare; one case was published by McKenna and Hines.<sup>24</sup>

Ultimate recovery depends upon the reversibility of the changes the blood vessels have undergone as a result of hypertension. One of the striking features of this condition is the clinical recovery after the removal of the tumor even after the symptoms of pheochromocytoma have been present for a considerable length of time. A remarkable regression of the manifestations has also been observed in the case described here.

#### SUMMARY

A case of pheochromocytoma is reported upon in which the paroxysms of hypertension had produced vascular changes characteristic of malignant hypertension, resulting in heart failure, a disturbed kidney function, and the typical manifestations of neuroretinopathy. Transient hyperglycemia and glycosuria were also observed. After operation on the left side had failed to produce results, the removal of the tumor which was on the right side caused distinct regression of the symptoms and manifestations of the disease.

The tumor was *visualized by tomography* after an unsuccessful search on the left side. The importance of tomography for the diagnosis and localization of adrenal tumors is pointed out.

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## SURGICAL OBSERVATIONS IN THE TROPICS

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**D**URING World War II, many surgeons without previous experience in tropical conditions and diseases have had to face new problems. Having years ago, myself, gone through similar difficulties, some of my observations may be helpful to others.

It is not my intention to dwell only on surgical tropical diseases; they are described in textbooks. I shall confine myself chiefly to pointing out a few diagnostic difficulties as they present themselves in connection with tropical or nontropical diseases under tropical conditions, and shall report also on a few original observations.

An interesting disease which can be very puzzling to surgeon and physician alike, if not conversant with tropical diseases, is *sprue*. The diarrhea associated with cachexia may be attributed to a colonic tumor or a chronic dysentery. The copious, frothy, acholic, fatty stools without slime and blood should lead to the right diagnosis. A tumor of the pancreas can be practically excluded by the absence of jaundice. I observed a case of sprue diagnosed as Grave's disease by a very experienced surgeon. The rapid pulse was caused by secondary anemia. A thyroidectomy nearly cost the patient her life. A single inspection of the stool cleared the diagnosis. The personal inspection of the stool in the bedpan and not in the bottle, in all diseases of the gastrointestinal tract, cannot be overemphasized.

In my experience I have found that sprue reacts to pancreatin treatment promptly and better than to any other therapy. It is my conviction, in spite of negative post-mortem findings, that the pancreas plays an important part in the pathology of sprue, a view which is contrary to orthodox opinion.

A very disturbing factor in surgical diagnostics in the tropics is *dysentery*. An example of this is illustrated in Case 1.

CASE 1.—A woman, 30 years of age, who was seen one night, gave a history of sudden abdominal pain with vomiting. She had no stool for two days, and normal, regular stools before. Temperature was 103° F., leucocyte count 25,000. There was definite guarding and sensitivity in the right iliac fossa; Rovsing's sign was positive. Diagnosis was acute appendicitis. Immediate operation showed that the appendix, cecum, gall bladder, and genital organs were normal. The case was puzzling until the next morning, when the patient had twenty to twenty-five typical dysenteric stools with slime and blood. Culture of stool showed Shiga-Kruse bacilli. The patient made a perfect recovery in spite of the operation.

The error in this case was comprehensible. No diagnosis of dysentery could be made in a patient with no previous history of diarrhea and with normal stool. The localizing signs were manifestations of an acute inflammatory process of the cecum, which could hardly be distinguished from those of the appendix.

While Case 1 shows that dysentery may make its appearance first in the ileocecal region, Case 2 reveals that dysentery may disappear from the colon while persisting in the appendix.

CASE 2.—A woman was treated during three weeks for dysentery of the Flexner type. She appeared completely recovered and returned to work, when suddenly, two weeks after recovery, she developed typical signs of an acute appendicitis. At operation an acutely inflamed appendix with serous exudate was found. Examination showed a perfectly normal mucosa of the ileocecal junction and the adjacent distal 5 mm. of the appendix, while the whole distal mucosa showed signs of a pseudomembranous inflammation, typical of dysentery (crimson red base and dark olive green mucosal ridges). Bacteriologic examination showed Flexner bacilli on culture.

One of my most serious blunders was an unrecognized intussusception, described in Case 3.

CASE 3.—A child 3 months of age had a history of three to four slimy bloody stools a day. Dealing constantly with dysentery in the tropics, one is tempted to think of the obvious. Finding no signs of obstruction, dysentery was diagnosed and treatment rendered accordingly. Only after two days, when the child started vomiting and developed signs of obstruction, did it become clear that there was an intussusception. By that time, the general condition of the child had become so poor that an operation appeared futile.

Even today, in full knowledge of Case 3, I should sometimes find difficulty in making the differential diagnosis between dysentery and intussusception under tropical conditions. The facts that the intussusception is frequently not palpable and that dysentery itself may produce intussusception make discrimination the more difficult.

One frequently hears that chronic appendicitis is commoner in the tropics than in Europe. The reason given is the frequency of amebic dysentery. In my experience, I have found that chronic appendicitis is hardly more frequent in the tropics than in temperate climate.

The diagnostic difficulties caused by amebic dysentery were described recently by Morgan.<sup>8</sup> The differential diagnosis between chronic amebic dysentery, diverticulitis, and colonic cancer is often extremely puzzling, especially in view of the fact that the presence of one of them does not exclude the others. Sigmoidoscopy, bacteriologic examination, and x-ray examination will often, but not always, clarify the situation.

Another infectious disease which frequently offers difficulties to the surgeon is *typhoid*. (Although it is not an exclusively tropical disease, it is much more common in the Tropics than in Europe.) I have often had the opportunity of observing an alarming sign which I have not seen mentioned in textbooks and which can be very misleading. In the second or third week of the disease, patients suddenly develop very violent pain, with guarding, in the left hypochondrium. This may easily be taken for a perforated typhoid ulcer or a splenic abscess, and a decision to operate in the usually poor general state of the patient may prove fatal. I have never actually operated for this complication, but seriously considered the necessity. It is my strong conviction that this acute pain is due to overstretching of the splenic capsule due to

acute splenic enlargement. It is probably the rate of enlargement that determines the sudden pain. It lasts one to three days and recedes gradually. I have also seen it repeatedly, during an attack of malaria. It goes without saying that once the cause of the pain is recognized, surgical interference should be avoided.

Another surgical complication of typhoid that I did not find mentioned in the literature, and which I observed twice in Chinese children suffering from very severe typhoid, is the partial or complete necrosis of the serotum. The testicles become completely exposed. In both these children the general condition was so poor that surgical interference was contraindicated, but I can imagine that under more favorable circumstances a temporary transplantation of the testes into the abdominal wall with later view of plastic operation should be considered. The cause of the necrosis is probably embolism or an endarteritis, aided by poor circulation.

*Actinomyces* plays a more important part in the pathology of abdominal and general surgery in some parts of the Far East. Japan for example, than in Europe. During my visit to the Kyoto Surgical University Clinic I saw two or three patients with abdominal actinomyces in one ward. The possibility of actinomyces should be borne in mind in long-standing hard infiltrations of the abdomen, especially those of the ileocecal region. Multiple sinus formations with the typical druses make the diagnosis obvious.

The gastric form of *malaria* with epigastric pain, vomiting, and occasional icterus can be very deceptive and mistaken for an acute cholecystitis, appendicitis, or obstruction. The history of recurrent rigors and fever, the large spleen, and blood examination will lead one into right channels if the possibility of these apparently surgical manifestations of malaria are remembered.

A question which, so far, is more of theoretical than practical significance is the etiologic relation of Buerger's disease to *typhus*. It was found (Goodman<sup>4</sup>) that in a very high percentage of patients affected by Buerger's disease, the Weil-Felix reaction was positive, and that most of these patients went through a typhus infection previously, hence, the high incidence of Buerger's disease among Polish Jews, etc. It will be of interest to see whether the infestation with typhus of the vast population of Italy, previously free of this infection, will show an increased incidence of Buerger's disease.

A very marked exophthalmus is another complication of typhus. It occurs in very severe cases only. It is rare and can be misleading. I saw several such complications during World War I in Rumania. I do not know whether this exophthalmus regresses later or is of a permanent nature. It is important that it should not be attributed to hyperthyroidism and should not be treated surgically. The cause of this sign in typhus is probably that the sympathetic nervous system is grossly affected by the infection, as shown by Abrikossoff.<sup>1</sup>

An interesting disease which is practically unknown in Europe but common in the Far East is *myositis purulenta*. It may be instructive to describe my first experience with it (Case 4).

CASE 4.—A young man 20 years of age was brought into a Chinese Hospital with what was considered to be a tuberculous psoas abscess. It was of immense size, indolent, and caused only a small rise of temperature. Although the primary focus could not be found, the diagnosis appeared certain and an assistant was reprimanded for incising the abscess. Surprisingly, the abscess, which contained several pints of creamy pus, healed completely in two weeks without leaving any sinus.

Soon after this, I saw another large abscess of the abdominal wall, tracing down the rectus, which I took again for a cold abscess originating from the ribs. My assistant again opened it without consulting me and again proved to be correct. Microscopic examination of the pus showed staphylococci. I realized then that these "cold abscesses" were something new to me and started collecting my observations, when similar cases were published by Osawa<sup>9</sup> in Osaka. He found that these abscesses develop in individuals suffering or having suffered from beriberi. On re-examining my material, I could confirm his observation in several, although not all, of my patients. They showed signs of peripheral neuritis (anesthesia, paresis) and dilatation of the right heart. Thus, the myositis purulenta is an avitaminosis B. Muscle which normally is resistant becomes liable to *Staphylococcus aureus* and *albus* infection. Osawa succeeded in producing muscular abscesses by injecting staphylococci intravenously into pigeons and rabbits fed on vitamin B-free diet.

The knowledge of this disease seems to me of great theoretical and practical interest. I should not be surprised if myositis purulenta appeared also in the underfed European population during or after World War II. These abscesses must be incised like any other nontuberculous abscesses and vitamin B must be given.

Leeham-Green and Winston<sup>6</sup> described this disease recently in Africa without, however, referring to its etiology. Myositis purulenta observed by me is probably identical with the tropical pyomyositis reported by Manson-Bahr.<sup>7</sup>

A technical advice which I missed in textbooks concerns the treatment of elephantiasis due to filariasis. The skin of elephantiasic legs and scrota is usually extremely hard and thick. If the skin is excised in this state the results are very unsatisfactory because too little of the infiltrated skin can be excised to make a marked difference and also the healing conditions of the thick skin are poor. The patient, should, therefore, be put to bed and his bandaged legs elevated for one or two weeks. It is surprising to see then how much of the thickening was due not to fibrosis but to accumulation of lymphatic fluid. The skin becomes more supple and hangs in large folds. One should then proceed with the operation. The method of choice is that of Payr-Kondoleon, which consists of excision of the excess skin and underlying fascia. The results so obtained are satisfactory.

The criminal injuries of a country often reflect the local customs, morals and living conditions and are, therefore, of interest from different angles. In Celebes I was told that liver and other abdominal injuries are extremely frequent. The reason for this is that people live in light bamboo houses, built off the ground on poles and, therefore, the vengeful neighbor can easily discover

TABLE I

CASE NO.	AGE (YR.)	TIME INTERVAL (HR.)	CONDITION ON ADMISSION	SHOCK	ANESTHESIA	DEATHS
1	23	2	Poor, comatose; dilated fixed pupils	None, B.P. 124/88	Local procaine	48 hr. P.O.
2	34	7	Conscious; associated injuries of chest and extremities	None, B.P. 136/66	Gaseous oxygen-ether endo-tracheal	
3	26	11	Poor, comatose; de cerebrate rigidity	None, B.P. 140/84	Local procaine	6 wk. P.O.
4	?	12	Poor, comatose; Cheyne Stokes respiration	None, B.P. 120/30	Local procaine	24 hr. P.O.
5	32	37	Poor, comatose; Cheyne Stokes respiration	None, B.P. 130/88	Local procaine	10 hr. P.O.
6	19	3	Poor, comatose; gunshot wound, perforation of skull	None, B.P. 125/60	Local procaine	48 hr. P.O.

fixed pupils, both of equal size, and a right sided hemiplegia. On removing the dressing a large amount of cerebral tissue was found incorporated in the gauze and more was herniating. The missile, a rifle bullet, had perforated the skull going from the right temporal through the left parietal bones. X-ray revealed a bursting type of fracture, involving the right temporal and left parietal bones across the midline. He was considered nontransportable and prepared for surgery. Preoperatively, one unit of plasma and 1,000 c.c. of blood were given. The anesthesia used was local procaine supplemented with 0.5 Gm. of sodium pentothal. The wounds of entrance and exit were excised and united across the midline by a linear incision 14 cm. long. The skull was extensively fractured, several large fragments being lifted away. There was great destruction of the dura and brain substance. The longitudinal sinus being severed necessitated a complete ligation. Profuse bleeding was encountered from torn cortical veins and several branches of the right and left middle cerebral arteries. These bleeders were controlled by the use of cautery and silver clips. The macerated brain tissue was then resected bilaterally, approximately 200 Gm. of brain substance being lost. The dura was left open since its complete exposure would have necessitated removal of almost the entire calvarium. The scalp was closed in two layers without drains.

Postoperatively, the patient did poorly and at no time did he recover consciousness. It was necessary to tube feed him. Lumbar puncture revealed no increase in pressure and the fluid was only slightly blood tinged. He died on the second postoperative day. Post-mortem revealed generalized softening and hemorrhages.

The results indicate the ineffectiveness of surgery in this type of injury. In other words, if a patient has sustained a brain injury severe enough to make him nontransportable, early surgery will not save his life. This experience further indicates that the field hospital is not the proper place for a neurosurgical team to function.

#### THE EVACUATION HOSPITAL

The evacuation hospital is the place of choice for early definitive neurologic surgery. Sixty-one patients of the entire series were seen and operated upon in this type of hospital.

TABLE II

NO. OF CASES	AVERAGE TIME LAG	DEATHS	PERCENTAGE DEATHS
61	19 hr.	7	11.4

These sixty-one cases will be analyzed from the standpoint of time interval, optimum conditions for surgery, anesthesia, procedures of choice, complications, and postoperative care.

## TIME LAG

It had been thought that any wound more than twelve hours old did not lend itself to primary closure. Table III indicates that the average time lag, that is the interval from wounding to operation, was beyond the twelve-hour period set down as safe for primary closure. The wounds were primarily closed in all sixty-one patients regardless of time lag. The patient with a seventy-six hour interval was treated in the same fashion as the one with only a two-hour interval. Thirty of these cases were followed to, and through, evacuation to the Zone of Interior. Of these wounds, all primarily closed, only one was re-operated upon for infection in a base hospital. The two other infections in this series developed while the patient was still in the evacuation hospital. Cultures in these two cases showed the presence of gram-negative bacilli, probably of the colon group. These two were under routine penicillin therapy and they responded to open drainage of the wound.

TABLE III. COMPLICATIONS AMONG THE THIRTY CASES

NUMBER OF CASES	SHORTEST LAG	LONGEST LAG	AVERAGE LAG	INFECTIONS	SULFONAMIDE ONLY	PENICILLIN
30	2 Hr.	76 Hr.	20.3	1	11	19

Eleven of these thirty patients were given sulfadiazine prophylactically, by mouth if conscious, intravenously and later by lavage if comatose. In none of the group was sulfanilamide used locally to the brain. Nineteen received routine penicillin and no sulfadiazine; the dose of penicillin given was 25,000 units intramuscularly every three hours for four days. Rammelkamp and Keefer\* have shown that penicillin given intravenously is not excreted in the normal cerebrospinal fluid. In spite of the questionable effectiveness of penicillin in cerebral injuries, the results were essentially the same, as in those where sulfadiazine was used.

Time lag and chemotherapy, although important, are not the deciding factors in primary closure. Thorough radical débridement is the single most important factor in the prevention of infection. This is best illustrated by Case 7.

## CASE REPORT

CASE 7.—A patient was seen twenty hours after injury. On admission, he was deeply comatose, had a left hemiplegia, and a large ragged wound of the right parietal area. His

\*Rammelkamp, C. H., and Keefer, C. S.: Absorption, Excretion and Toxicity of Penicillin Administered by Intrathecal Injection. *Ann. N. Y. Acad. Sci.* 1943, 45: 1-15.



pupils were equal and reacted to light. Surgery was performed under local procaine field block. The wound was excised and enlarged. The skull defect 2 cm. in diameter was enlarged to 5 cm., thus exposing normal dura with a central defect through which brain substance was herniating. A small extradural clot was evacuated. The tract in the brain was 10 cm. deep. All devitalized brain along the tract was excised and an intracortical accumulation of blood was removed under direct vision. Four indriven bone fragments were removed. The foreign body was not visualized and was left in place. The field was dry and the brain pulsating normally on completion. The dura and scalp were closed in layers without drains. By the fourth postoperative day the patient had improved sufficiently for evacuation to the rear.

*Follow-up Note.*—The patient was received at a station hospital and then sent to a general hospital. Here he was found to be stuporous. The wound was bulging and lumbar puncture revealed marked increase of intracranial pressure. He was re-operated upon on the twelfth postoperative day and a small deep right temporal abscess in a small hematoma (subdural) was found and evacuated. Two months later he was evacuated to the Zone of Interior, having made excellent and rapid improvement. This patient received routine penicillin therapy (nonlocally). The infection was in a hematoma which either was missed or had accumulated after surgery. In other words, the initial surgery had been inadequate and the presence of old blood provided the nutrient material for bacterial growth.

It is felt that the time interval, although important, does not preclude definitive surgery and primary closure of the head wound. The local application of either sulfanilamide or penicillin is not essential. Therefore, adequate radical extirpation of all devitalized brain, accumulation of blood, and bone fragments is the answer to the prevention of infection.

SHOCK

In preparing the patient for surgery, the presence or absence of shock is the prime consideration.

TABLE IV

DEGREE OF SHOCK	PRIOR TO ADMISSION	ON ADMISSION	ASSOCIATED INJURIES	DEATHS
Mild	16	8	3	3
Moderate to severe	10	1	6	2
None	35	52	18	2

Table IV is a compilation of the number of patients in shock prior to, and on admission to, the evacuation hospital. The patient was considered to have mild shock if only one or two units of plasma were needed to restore him. Those patients needing three or more units of plasma or blood were considered to have been in moderate to severe shock. Of the twenty-six patients treated for shock prior to admission, only nine exhibited any evidence of shock on admission to the evacuation hospital. It is further noted, that of the ten patients considered to have been in moderate to severe shock, six had associated injuries to the abdomen, chest, or extremities. The shock associated with head injuries is due to blood loss and is comparatively mild. This form of shock is easily combated with plasma, blood, fluids, and warmth. Severe shock, as seen in patients with wounds other than the head, is rarely seen in uncomplicated cranial injuries. Severe head injuries exhibit signs of embarrassment related to the vital cerebral centers. These signs are hypertension, slow pulse, cyanosis, and

TABLE V

TYPE	NUMBER	TYPE PATIENT	DEATHS
Local procaine	23	Comatose or stuporous	7
Local procaine and sodium pentothal	24	Good condition and conscious	0
Gas oxygen ether endotracheal	14	Poor condition or face down position	0

rising temperature, and are usually due to increased intracranial tension. The treatment is relief of the increased intracranial tension by surgery.

#### ANESTHESIA

The choice of anesthetic agent depends upon the patient's condition and the length of time necessary for surgery. Table V indicates that the three methods were fairly equally distributed. With patients who were conscious and in good condition, and the surgery took sixty minutes or less, local procaine supplemented by sodium pentothal was used. The amount of pentothal needed rarely exceeded 1.5 Gm. The use of a general anesthetic in all conscious patients is to be preferred as the mental shock of a craniotomy is not to be underestimated. Patients have a tendency to magnify the extent of their cranial defect if conscious during the débridement of the skull. Endotracheal gas-oxygen ether is reserved for operations of long duration, or where the patient is face down on the table. It is also used in those patients having respiratory difficulty since it allows for an open clear airway and forced respirations may be easily instituted. Local procaine regional block was used in all comatose or stuporous patients not falling in these two categories. Although it is true that local procaine is safest, it not only is bad psychologically in the conscious patient but also tends to limit the operator. If the patient is awake, the tendency to be conservative in the surgical procedure is strong and adequate débridement not accomplished.

#### SURGICAL PROCEDURE

To discuss all varied procedures is not within the scope of this paper. It is of great importance to provide adequate exposure not only of the skull defect but also of the brain injury. The difficulties arising in débriding the brain and controlling bleeding stem primarily from inadequate visualization.

The first step is excision of the involved scalp and periosteal edges with extension of the wound to afford good exposure of the skull defect. The scalp bleeding can be controlled with a few clamps to the galea and placing of self-retaining retractors. In this series the tripod incision was not used. All were linear or curved linear incisions.

The involved dura and brain can be adequately exposed by enlarging the defect in the skull with rongeurs. The usual wound has indriven bone and the brain is macerated and herniating. The herniation is due to indriven bone and intracortical bleeding. It is found that the presence of intracranial hypertension increases the vascularity of all the structures above the brain. It

advisable to control this oozing with cotton packs and continue the surgery until the intracerebral pressure is reduced. This will result in complete control of all oozing and cut down the time spent in attempting to control the bleeding initially.

Dural trimming should be minimal. In most instances the dura, although lacerated, is relatively clean. The débridement of the brain must be thorough and under direct vision wherever possible. Blind suction or manipulation is best avoided because any bleeding resulting from the procedures is not only difficult to control but increases the brain damage. Clean resection under direct vision, making use of lighted retractors, tend to lessen loss of functioning viable brain tissue. It is also best to avoid blind probing for the removal of metallic foreign bodies. If the foreign body is too deep to be reached with lighted retractors, it is best left in place and the tract down to the foreign body resected. The use of the cautery should be minimal. In potentially contaminated wounds, all devitalized material left by cauterization tends to favor the growth of organisms. This is especially true when the scalp or periosteum is cauterized. The soft rubber catheter is of great value in localizing bone fragments and metallic foreign bodies and in aspiration of devitalized material of the brain. The introduction of fluid under pressure through the catheter is to be avoided, since it will result in the spread of the fluid and contaminated material into the interstices of the brain substance, thus adding insult to an already damaged brain. It is imperative that all indriven bone fragments, hair, and dirt be removed. The stereoscopic x-ray films are most valuable in the localization of bone fragments. Here again the lighted retractors are indispensable aids in eliminating blind probing and illuminating all side pockets containing nests of bone fragments. The control of bleeding is made simple by visualization of the bleeding point. This is best done by applying gentle suction and bringing the bleeding vessel up for clip or cautery. In generalized oozing, if not due to continued intracranial tension, a warm moist cotton pack will be effective. These warm packs are most effective if left in place for at least three minutes. A torn venous sinus lends itself to control if well exposed. The overlying bone should be removed rapidly and sufficiently to expose the entire tear. It can then be dealt with, either by ligation or the application of a small muscle stamp. It is important to be bold in the control of hemorrhage, since less blood is lost and less damage produced if the bleeding point, or vessel, is directly attacked. Dural bleeding from beneath the bone edges can be controlled by one or more sutures from the dura to the periosteum, thus drawing the dura up to the overlying skull.

If after adequate resection of the tract there is still intracranial tension, an accumulation of blood should be looked for. This accumulation may be on the same and, not infrequently, the opposite side, or both. A case in point is Case 8.

#### CASE REPORT

CASE 8.—A man, aged 23 years, was seen two hours after injury. On admission he was comatose with unequal pupils, the right being larger than the left and both fixed to light.

There was a large ragged left parietal wound with marked cerebral herniation. X-ray revealed a 2 cm. foreign body in the left parieto-occipital lobe and marked stellate fracture of the left parietal bone. In addition, there were many superficially indriven bone fragments. Craniotomy was performed under local procaine field block. The brain was found to be very tense and extradural and subdural blood was searched for but not found. The herniating brain and tract were resected and all indriven bone was removed. The foreign body was too deep to be visualized and left in place. The brain was still tense when the wound was closed. Postoperatively, the patient did poorly and in view of the dilated right pupil, he was reoperated upon the next day. A right subdural hematoma of approximately 30 c.c. was found. When this hematoma was evacuated, the brain appeared to be under normal tension and nothing further was done. His condition did not improve and he died on the third postoperative day. Post-mortem revealed that in addition to the former subdural hematoma, the right parietal lobe contained a large 50 c.c. intracortical hematoma, approximately 2 cm. deep.

Case 8 illustrates the importance of investigating for the presence of hematomas in continued intracranial tension. These hematomas may be extradural, subdural, intracortical, or ventricular. In those cases where the foreign body crosses the midline, intraventricular hemorrhages are frequently the cause of death and they should be dealt with. Table VI illustrates the number of patients in this series with concomitant hematomas and their location.

TABLE VI

TOTAL CASES IN SERIES	SUBDURAL	EXTRADURAL	SUBDURAL AND EXTRADURAL	INTRACORTICAL
61	8	2	2	13

In this series of sixty-one cases there was a total of twenty-five complicating hematomas, or a percentage of 41.

The dura should be closed in all instances if at all possible. There are cases where the destruction is so extensive that it would necessitate removal of most of the calvarium to place a patch. It was found that the periosteum in the operative field usually sufficed. Having marked elasticity, a small piece can be stretched over a large defect in the dura. In only two cases was it necessary to obtain a piece of fascia lata for the repair. In the closure of the scalp, the prevention of tension is most important. The vascularity for which the scalp is noted facilitates excellent healing, if not interfered with. Tension results in avascularity and the resultant breakdown of tissue provides fertile ground for bacterial growth. Where there is marked destruction and loss of scalp, a sliding scalp flap is the procedure of choice. The flap should be approximately three times the size of the scalp defect. On sliding the flap toward the defect, a denuded area of periosteum is left. The size of the denuded area may be decreased by bringing the unattached edges of scalp as closely together as possible and placing a row of sutures from the galea to periosteum. This maneuver tends to seal the denuded area from the original wound and to delineate the exudate that forms here. The exposed periosteum is then covered with a Thiersch graft from the thigh.

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#### CASE REPORT

CASE 8.—A man, aged 23 years, was seen two hours after injury. On admission he was comatose with unequal pupils, the right being larger than the left and both fixed to light.

## WARTIME NEUROSURGICAL EXPERIENCES

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AN ANALYSIS and classification of 342 penetrating brain wounds has recently been published.<sup>1</sup> This was further broken down into a report of 100 ventricular wounds and again into 159 extensive brain wounds.<sup>2, 3</sup> The experience and circumstance surrounding the compilation of this series prompt this communication. The objective presentation of technique and results of wartime brain surgery does not permit generalization or editorial opinion. Such latitude may be allowed in a personal report of experiences.

During the period described, in addition to operating upon some 400 patients with penetrating brain wounds, it was necessary to care for and operate upon well over 100 penetrating skull wounds, or ordinary compound or depressed, skull fractures. Hundreds of simple scalp lacerations were repaired. Over 100 spinal cord wounds were laminectomized; 62 brain abscesses and 31 cerebral fungi were operated upon. Some 300 peripheral nerve lesions were repaired. This constitutes a surgical experience of over 1,100 surgical procedures, most of which was accomplished from D day, June 6, 1944, to the cessation of the war with Germany, May 8, 1945.

The great majority of this was done in evacuation or field hospitals, at or near the front lines. Work on the beach heads was done in clearing stations and the later work, on abscesses and peripheral nerves, was done in a general hospital.

The foregoing is submitted, in all humility, as an experience in which some of the wartime progress in the field of neurologic surgery was seen to unfold and is intended only as a basis for the propagation of observation.

*Previous Concepts and Early Neurosurgical Treatment.*—The outbreak of World War II found the world's neurosurgeons with nothing to add to Cushing's methods of World War I.<sup>4, 5</sup> The Spanish Civil War had not promulgated any radical changes. The English contributions, from 1939 to 1941, in the form of their splendid attempt to furnish early, trained care by mobile neurosurgical teams, had resulted in some lowering of the mortality and morbidity. Aseroft's series<sup>6</sup> of 292 penetrating brain wounds had emphasized some long-known truths. It was found that neurosurgery must be early, primary, and definitive. This remained a cliché, however, and its tremendous importance was not fully realized.

The number of qualified neurologic surgeons in the world is small. Therefore, to allow good care, at the most important stage, well-grounded general surgeons, young, to withstand the rigors of the field, had to be trained in

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neurosurgical principles. This was done forthwith, and some of these men have made a notable record of achievement.\*

Cushing's experiences with 133 brain wounds in World War I left us with the concept of brain débridement, definitive surgery, and primary, complete closure. His postoperative mortality was 37 per cent, largely due to infection. He turned bone flaps to better visualize the pathology, popularized the spider and tripod scalp incisions, relied upon a galeal closure, and did not emphasize a dural closure.

*Specific Advances in Neurologic Surgery.*—The improved results of brain surgery in World War II can hardly be attributed to an improvement in technical dexterity. It is felt, however, that the adjuncts of surgery have allowed us to venture into recesses of the brain hitherto forbidden, and have allowed procedures to be planned and carried out successfully that formerly would have ended only in disaster. The electrocautery and portable suction machine, lighted brain retractors, fibrin foam, and penicillin contribute more than any other adjuncts. Anesthetic agents, silver clips, sulfonamide drugs, plasma, and suitable instruments all make their contributions. Our armamentarium, in the Mediterranean theater, was lamentable. As our knowledge of war increased, so did our knowledge of military surgery and the necessary items were unhesitatingly supplied. Never, during the height of the European campaign, were we lacking in any necessary item.

Brain wounds, in World War II, have been classified as to prognosis, type, location, and treatment. Surgical adjuncts, not available to Cushing, have allowed the mortality rate to be reduced to 12 to 15 per cent. The infection rate has been reduced to 10 to 15 per cent. Only 4 to 7 per cent of patients with these infections die.<sup>1</sup>

The fallacy of any scalp incision allowing poor blood supply to the tissue was borne out. Swinging or sliding scalp flaps were found to be preferable. Skull defects are repaired with tantalum plates. Primary tight closure is a necessity, but the absolute necessity for dural closure is borne out when secondary operations are done at a later stage. Free periosteal, temporal fascia or fascia lata graft, or a sliding, attached pericranial graft can be used to repair dural defects. Cadaver dural repairs have not been successful.

Adequate resection of missile tract to healthy brain, including all bone fragments, is of vital importance. There is no alternative to this dictum. A solitary bone chip may cause no trouble, but a cluster of three or four such chips is a focus around which an abscess may form. Metallic foreign bodies are removed, if large and if accessible. Small or inaccessible fragments are left in situ (Fig. 1).

Almost all of Cushing's patients with ventricular wounds died. This mortality was reduced during World War II, through a proper concept of pathology and necessary surgery, to less than 30 per cent.<sup>2</sup>

\*Brigadier Hugh Cairns, of the British Army, and our senior consultants of the American Army, Colonel Loyal Davis and Colonel R. Glenn Spurling, are deserving of high praise for their attempts, unceasing, and in the face of supply and personnel shortages, to carry out this single, all-important concept.

Unique approaches and techniques have allowed surgical repair of wounds formerly considered fatal. Removal of contralateral foreign bodies over the vault, with retrograde cleansing of the missile tract, has become commonplace (Fig. 2). Lobectomy necessitates, for radical removal of devitalized brain tissue, bone fragments, and foreign bodies, obviates scarring and removes a medium for growth of bacteria.

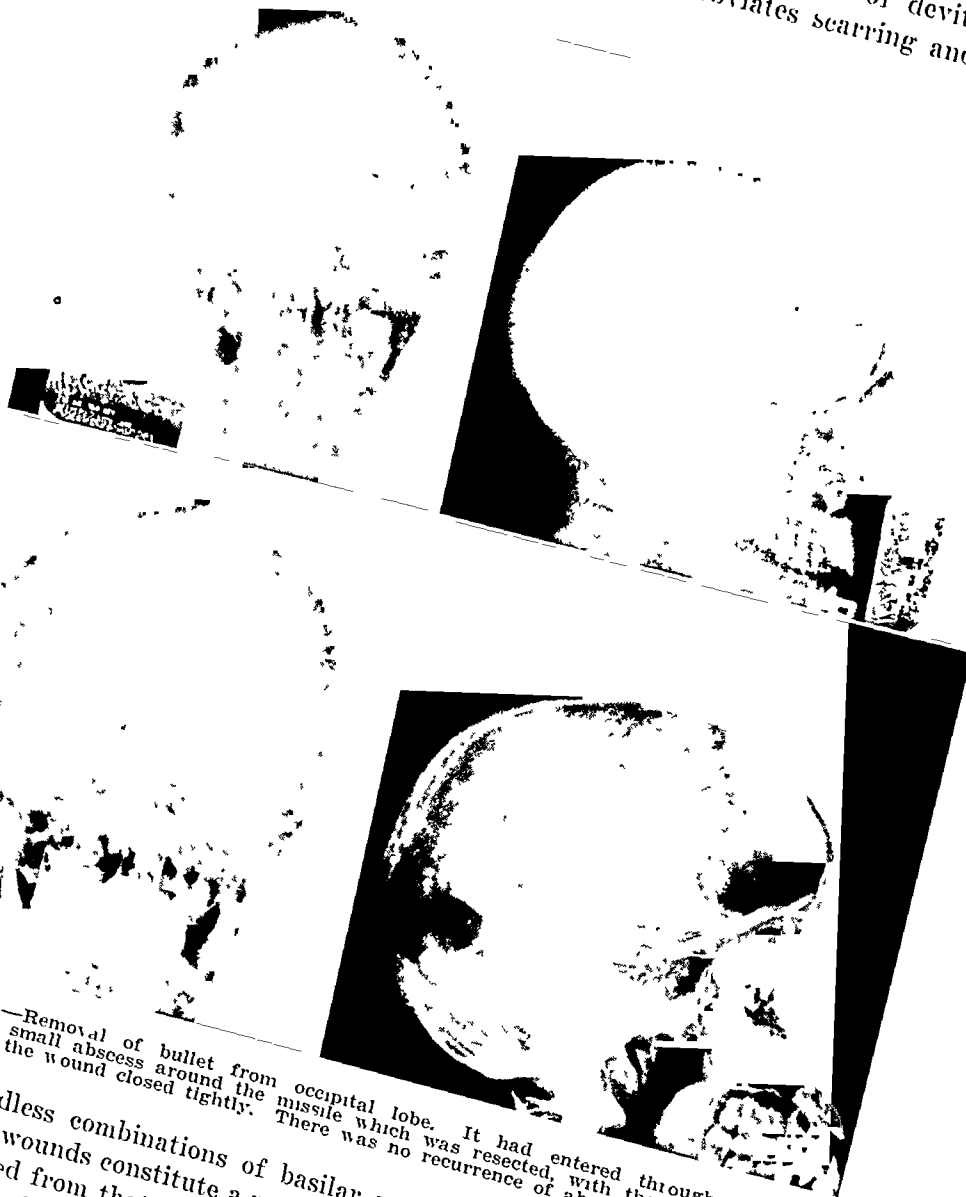


Fig. 1—Removal of bullet from occipital lobe. It had entered through the orbit. There was a small abscess around the missile which was resected, with the bullet, penicillin instilled, and the wound closed tightly. There was no recurrence of abscess after five months.

The endless combinations of basilar wounds, frontal plate wounds, and frontal lobe wounds constitute a major challenge to the surgeon. The problem is far removed from that of merely turning a frontal bone flap and grafting a dural defect. Some of the most major surgery of the war was done in these regions. The problem should be attacked with every possibility and every approach fully in mind.



Recently, a series of three subdural hygromas has been reported.<sup>7</sup> Since that time an additional twelve have been operated upon, and, during this time at least, found to be as frequent as subdural hematomas. Indeed, preoperative diagnosis does not seem as obscure or difficult as formerly supposed. All twelve patients lived and made a complete recovery.

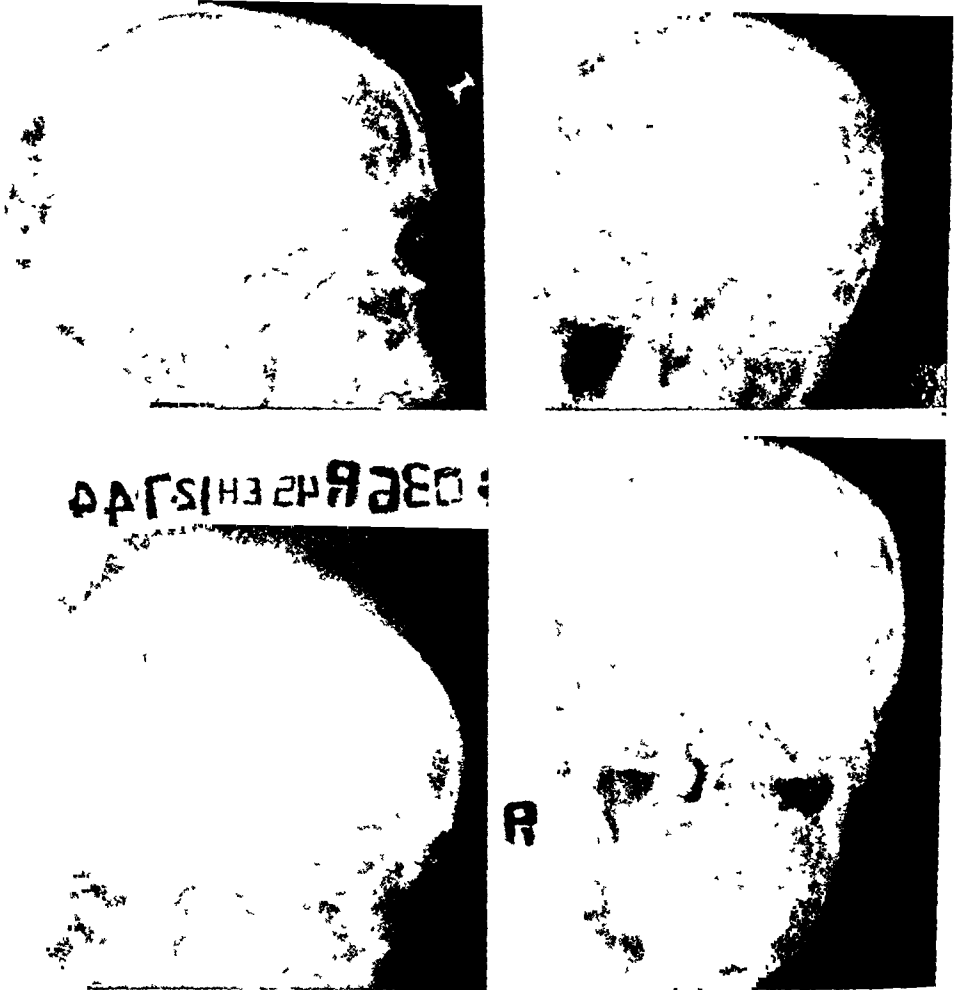


Fig. 2—Removal of contralateral foreign body over vault with retrograde cleansing of missile tract through brain.

Several cases are recalled, memorable because of technical difficulty or extent of pathology. Successful removal, during a particularly heavy bombing, of a large foreign body in the midbrain occasioned some tension. The cleansing of a missile tract through the occiput, cerebellum, base, and posterior fossa, to the internal carotid artery in the middle fossa was followed by recovery with no neurologic deficit.

Removal of one entire mangled frontal lobe and the tip of the opposite lobe, associated with the relief of a physiologic transection of the spinal cord, by laminectomy, seemed useful. Leg motion returned to this patient and the brain wound had caused little discernible defect.

A completely blind soldier had a large, midline, occipital fungus. This was resected, only to the point where distorted optic radiations were allowed to resume their function, and vision was restored, dramatically, while the patient was on the operating table.

It is firmly believed, and is the author's single outstanding concept that wartime neurologic surgery must be done very early, under seventy-two hours certainly, and under twelve hours, if possible. It must be complete and definitive at this time and, also, it must be the best possible procedure, done by a qualified neurosurgeon. The golden opportunity, utilization of which saves lives and avoids infection, lies in the first operation. This can be, and usually was, done within the first twenty-four hours and hundreds were done under twelve hours (Table I). Disposition of neurologic surgeons in evacuation hospitals allowed this. Mobile neurosurgeons, to operate on non-transportable patients in field hospitals, allowed care for this group, already suffering from serious abdominal or chest wounds.

TABLE I. INFECTION INCIDENCE AS DETERMINED BY TIME LAG BEFORE DEFINITIVE SURGERY\*

HOURS ELAPSED BEFORE SURGERY	PATIENTS	INFECTIONS	%
24	205	1	$\frac{1}{2}$
48	38	5	14
72	36	9	25
96	12	5	45
Over 96	31	25	80
Total	322	45	13.9

\*Penetrating brain wounds only. Infections consisted of abscesses, fungi, meningitis, and scalp infections.

Almost every instance of incomplete operation was followed by infection. Almost every patient, wherein the dura mater had not been closed, developed a fungus or an infection.

*Anesthesia.*—The advance of the specialty of anesthesiology in World War II can hardly be spanned in a paragraph. The combination of sodium pentothal and local infiltration of procaine has proved a remarkably efficacious one. Endotracheal administration has solved many problems concerning combined maxillo-facial-cranial wounds. Brachial blocks to allow peripheral nerve surgery and paravertebral sympathetic blocks in the treatment of causalgias constitute great progress.

*Penicillin and Sulfonamides.*—It is strongly felt that infections can be aborted early, with ease, by proper surgery and the local use of penicillin. It is equally strongly felt that if the surgery is incomplete or delayed, infections are inevitable and, if once developed, their cure is difficult.

Penicillin locally, prophylactically, is of extreme value and must be credited with the lowering of the infection incidence. There seems to be no other plausible explanation. It seems more effective than sulfonamides

when used locally.<sup>1</sup> Therapeutically, the effect on cerebrospinal infection is dramatic, and, because of it, hitherto forbidden techniques are now possible.

Penicillin- or sulfonamide-resistant strains, such as a gram-negative bacillus, may be made sensitive to the sulfonamides by the use of urea. The addition of this drug has shown promise.

Intramuscular penicillin, while crossing the blood-brain barrier into the cerebrospinal fluid in small amounts, has no great effect on central nervous system infections. It may obviate superficial scalp infections and Cairns believes that central nervous system infections start in this fashion. If so, then it is of value, administered by this means. If, however, a ventricular wound is sustained, or infection feared or present, direct instillation of liquid penicillin, full strength, into the cerebrospinal fluid or the ventricles, in large amounts (50,000 Oxford Units) gives dramatic results. Using it routinely, the author has seen no sign of irritation, reaction, or epileptogenic tendencies, and can only speak well of it.

It is believed that sulfonamides, locally, are of much less value than previously thought. Their local use, however, prophylactically, at the time of initial débridement of an extremity wound, seems to allow that wound to be secondarily closed in a shorter period and with safety. More important, it allows that wound to be reopened earlier, so that a peripheral nerve injury may be repaired. Local use of sulfonamides, secondary suture, and early proper repair of nerve lesions have afforded us the expectation of good results from peripheral nerve surgery. Of over 300 patients the author has operated upon for peripheral nerve lesions from three to six weeks after secondary closure, only three revealed residual infection. The pus, while present, was sterile, and surgery proceeded as planned, with no subsequent breakdown. This was felt to be due to local and systemic use of sulfonamides and post-operative penicillin.

*Spinal Cord Wounds.*—The results of early laminectomy in patients with spinal cord wounds seemed encouraging, in contrast to the old dictum that none survive. Despite clinical and roentgenographic evidence to the contrary, most spinal cords are anatomically intact, although physiologically severed. Laminectomy, then, may cause, and has in increasing number, a return of some function. Particularly is this true of cauda equina lesions. Laminectomy should be done at the first possible place in the chain of evacuation where a qualified neurosurgeon and reasonable facilities exist.

Many hemilaminectomies were done. This operation seemed suited for the removal of unilateral foreign bodies, unilateral spinal cord compression, or unilateral radiculitis. It seemed of particular value in cervical spinal cord wounds. By the wound's very nature, no patient with a wound of the cervical cord requiring a wide laminectomy survived. Twelve cervical hemilaminectomies were done for partial cord lesions and radicular syndromes (Fig. 3). All of the patients lived and function, of varying degrees, returned.

These controversial points, concerning spinal cord wounds, will be presented in another communication.

*Peripheral Nerve Surgery.*—Peripheral nerve surgery is included in the responsibility of the neurologic surgeon. The number of these lesions is very large and the problems presented are many. The results, however, are now so encouraging that a new era in the treatment of nerve injuries can be envisaged.

The result of suture of severed nerve ends has usually been disappointing. New adjuncts and a better understanding of pathology have changed this picture to one of considered optimism and now approximately 90 per cent chance of regeneration can be expected. Severed nerve ends do not allow an accurate approximation or estimation of nerve damage, in the acute stage. Three to six weeks, therefore, after the wound has been secondarily closed, the patient is re-operated upon and the nerve ends approximated with fine, nonreactive tantalum wire. The suture line and area of scar are protected by a tantalum foil cuff, minimizing tissue reaction. Under such ideal conditions, results are very promising. Nerve grafts have been disappointing and, in America at least, have fallen into disfavor. Plasma glue, to approximate nerve ends, has been used to advantage. The tantalum cuff, probably, is the biggest single factor in the success of this method of repair.



Fig. 3.—Cervical cord wound caused by foreign body at left of sixth and seventh cervical vertebrae. There was an artefact at the second cervical vertebra. Laminae of the sixth and seventh cervical vertebrae had been fractured and were compressing the cord. This was relieved by hemilaminectomy and removal of foreign body. Function returned.

All important nerve trunks have been accessible and have been repaired, even down to the digital nerves. The brachial plexus, from the cervical roots down, has been repaired with good results (Fig. 4). The lumbosacral plexus has remained, to the author at least, inaccessible.

Combined nerve-bone lesions are being attacked intensively, keeping the thought paramount that an arm with no nerve function is no better than a prosthesis. Accordingly, orthopedic results are thought of as being secondary to nerve repair. Failure to approximate a radial nerve because of a large gap in substance is overcome by shortening the humerus.

*Brain Wound Complications.*—The treatment of complications of brain wounds has undergone a particularly spectacular change. Meningitides have responded well to chemotherapy, although an occasional fulminating infection appeared sulfonamide- or penicillin-fast. No patient who had been adequately operated upon, early, who had undergone the precautions described, and who had received adequate penicillin and sulfonamide therapy developed an

A.



B

Fig 4—A, Repair of brachial plexus lesion, necessitating only neurolysis, at level of roots, above clavicle. Note tantalum cuff. B, Repair of brachial plexus at level of clavicle, necessitating section of clavicle and neurorrhaphy. Note tantalum around and under the plexus and wiring of clavicle.

infection. The implication, then, is clear, that this is the most important single step in the prevention of complications.

Brain abscesses, formerly one of neurosurgery's most pressing problems, are the subject of a new and daring approach. Despite an infected missile tract leading to the abscess, the entire mass including the capsule of the abscess is resected or removed, in toto. This may be done with the loop cautery. Large amounts of penicillin, up to 100,000 units, are instilled. The dura is closed tightly, the cranial defect plated, and the scalp closed in layers. The results have been remarkable and the mortality has been in the vicinity of 5 to 10 per cent. Obviously, if there is no attempt at encapsulation, and the infection is a diffuse cerebritis rather than an actual abscess, the area is packed, according to the method of King,<sup>8</sup> and allowed to extrude. Judicious combination of these two methods may allow an even greater decrease in mortality.

Cerebral fungus has also been attacked radically. These potentially infected, functionally dead masses of protruding cerebral tissue are resected with the loop cautery to healthy tissue. Penicillin is then instilled or insufflated and a tantalum plate is inserted to cover the cranial defect as well as to restrain the exuberant cerebral protrusion. Thus, the plate acts as a restraining dressing. No dural graft is necessary. Obviously, any pockets of infection are resected. The scalp is closed tightly. Increased intracranial pressure is controlled by judicious and repeated lumbar puncture. Thus, at one sitting, the problem of a large, fungating mass, usually requiring weeks or months of treatment and resulting in marked scar, is obviated. Suggested by Carmichael,<sup>9</sup> the procedure has been applied by all of us with excellent results.

Cranioplasty, at a more distant echelon, is almost exclusively accomplished by tantalum plates. They are easy to apply, malleable, and nonreactive. The result is excellent. Acrylic, while necessitating a first stage for the purpose of an impression, obtains an even better cosmetic result.

Neurosurgical centers were set up in the Communication Zone, where the secondary problems were handled. Complicating infections, bad results of primary surgery, cranioplasty, further postoperative care, and peripheral nerve surgery were studied and carried out. Additional larger neurosurgical centers, in the Zone of the Interior, carried this program a step further.

The specialty of neurologic surgery, in the history of war surgery, will not be exceeded in brilliance, attained results, and scientific technical advancement. The combination of superb training in the specialty, an abundance of matériel, judicious administration, daring technical advances, and surgical adjuncts such as penicillin, have contrived to write a new chapter. The knowledge derived from the unfortunate source of war may be gainfully applied to the demands of peacetime neurosurgery.

#### SUMMARY

1. Advancement of specialty of neurologic surgery in wartime is outlined.
2. Swift evacuation, very early, primary, definitive, and complete surgery is necessary to avoid later complications.

3. Reduction of mortality and morbidity rates from those of World War I is ascribed to new techniques, surgical adjuncts, and penicillin.

4. Later complications, such as abscesses and fungi, amenable to radical new procedures, are feasible because of penicillin.

5. Value of sulfonamides to allow early repair of peripheral nerve injuries is emphasized.

6. More encouraging aspect of spinal cord wounds is noted.

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# ANAEROBIC INFECTION AND GANGRENE OF WAR WOUNDS IN CASUALTIES FROM THE PHILIPPINE ISLANDS

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THE purpose of this report is to present an analysis of cases in which anaerobic infection or gangrene occurred as a complication of war injuries. Experience with thirty-seven cases is the basis for the analysis. The cases were included in a group of 4,040 surgical battle casualties admitted consecutively to this general hospital during the campaign for the Philippine Islands. Following their early surgical treatment in forward echelons these patients were admitted to this hospital five to twenty-one days after injury. Thus, the surgery of these casualties was concerned with the management of late complications. Anaerobic infection or gangrene complicated 0.9 per cent of the 4,040 surgical battle casualties. These have been reported upon elsewhere.

The mere finding of pathogenic clostridia in a wound is not of importance. However, it is of interest that *Clostridium welchii* was recovered from 13 per cent of all wound cultures. All wound discharges were cultured aerobically and anaerobically. The facilities were not available for identification of all clostridia. The determination of *Cl. welchii* was made by the use of the classical test of "stormy fermentation" of milk. Positive reactions for *Cl. welchii* were checked by two laboratories. The types and locations of wounds from which *Cl. welchii* was recovered on culture are of interest. These are presented in Table I. These 175 wounds represent 3.9 per cent of 4,391 wounds in the series of 4,040 casualties in which they are encountered.

That pathogenic clostridia contaminate certain types and locations of wounds is brought out by Table I. In the over-all analysis of 4,040 casualties from which these cases are taken the fractures of the tibia and fibula made up only 13 per cent of all fractures. However, fractures of the tibia and fibula accounted for 33 per cent of those compound fractures which were contaminated with *Cl. welchii*. Similarly, fractures of the femur, of the bones of the ankle and foot, and of the scapula were contaminated with *Cl. welchii* in a higher percentage incidence than is indicated by the relative frequency of occurrence of these fractures. Wounds of the buttock comprised only 5 per cent of all soft tissue wounds, while 56 per cent of those contaminated with *Cl. welchii* were wounds of the buttock. Seventy-five per cent of the wounds from which *Cl. welchii* was recovered were those in association with compound fractures. The thirty-seven patients in whom clinical gas infections or gangrene occurred constitute 0.91 per cent of the group of 4,040 battle casualties and 21 per cent of wounds contaminated with *Cl. welchii*. The incidence of true gas gangrene was 0.33 per cent while anaerobic cellulitis occurred in 0.56 per cent of battle casualties. The cases have been classified clinically as shown in Table II. No streptococcal myositis was encountered.



TABLE I. WOUNDS CONTAMINATED WITH *Cl. Welchii*

TYPE	NUMBER	PER CENT
Compound fracture		
Tibia and fibula	44	33.3
Femur	32	24.2
Bones of ankle and foot	20	15.0
Radius and ulna	15	11.3
Scapula	13	9.8
Ribs	4	3.0
Femur and tibia (knee joint)	3	2.2
Acromion	1	0.8
	132	99.6
Wounds of soft tissue		
Buttocks	21	56.0
Thigh	4	10.8
Calf	3	8.1
Axilla	2	5.4
Foot	2	5.4
Shoulder	1	2.7
Arm	1	2.7
Chest wall	1	2.7
Abdomen	1	2.7
Sacroiliac region	1	2.7
	37	99.2
Wounds of large bowel or rectum	6	
Total	175	

*Clostridial Myositis*.—Included in the group of patients with clostridial myositis were eight in whom the gangrene was limited to particular muscles or groups of muscles and six in whom all muscles of the extremity were involved in the spreading, necrotizing process. Primary injuries in these fourteen patients were as follows: compound fracture of the femur, 7; tibia and fibula, 5; scapula, 1; soft tissue wound of thigh, 1. In contrast to the usual history of sudden onset of this disease within a few hours or days after injury, the lapse of time between injury and onset in this group averaged ten days. In all of these patients the casts were stained and smelly. In eight the complication was in evidence on first inspection of the patient. In six cases the onset followed the institution of skeletal traction. Twelve of the fourteen patients had been treated continuously with penicillin from the time of débridement until admission to this hospital. In twelve of the fourteen débridement had been done under six hours. In one-half of these the small incisions suggested that débridement may not have been adequate. In two cases there was no record that débridement had been done. The chain of symptoms and findings in these cases is as follows: acute onset, very severe toxemia, severe pain at the site of the injury and in the extremity distal to the point of injury, restlessness, thirst, tachycardia, fever, marked swelling of the extremity, cadaveric pallor of the skin of the extremity, and serous exudate with or without gas bubbles from the wound.

TABLE II. ANAEROBIC INFECTION AND GANGRENE OF WAR WOUNDS

	NUMBER OF CASES
Gas gangrene (clostridial myositis)	14
Anaerobic cellulitis	23
Total	37

There may be a bronzed tint to the skin of the face, upper chest, and arms. Crepitation of the tissues was present in six patients and absent in eight. Roentgenogram showed gas in the tissues in four of the eight cases in which x-ray views had been taken. Peripheral pulses of the affected extremity were absent in six patients, weak in two, and normal in six.

Eight cases are classified as localized clostridial myositis. In these the hemorrhage and necrosis were limited to one or more muscles or group of muscles. Actually these were virulent infections in which the disease was interrupted surgically before all muscles of the extremity were involved. At the time of operation the involved musculature was dark brown and noncontractile in four patients, altered by patchy necrosis and hemorrhage in four. In these patients the muscle became gangrenous by regional extension of anaerobic infection from a latent abscess in the tract of the missile. Operative therapy consisted of wide incision and drainage combined with excision of all of the gangrenous musculature. In two of the eight patients amputation was necessary. Intensive penicillin therapy was given after operation in all cases. It had no apparent effect on the toxemia or upon the course of the fever. Gas gangrene antitoxin was given to six patients after operation in doses of 10,000 units every four hours. On the fourth day it was discontinued because of severe urticaria. One patient died in toxemia following a long illness complicated by hemorrhage from the wound and gangrenous cholecystitis. The other seven recovered following radical excision of muscle groups. Case 1 is a report of a case in which localized clostridial myositis developed from an abscess.

#### LOCALIZED CLOSTRIDIAL MYOSITIS

CASE 1.—A private in an infantry regiment was wounded in action by enemy artillery fire Feb. 16, 1945. Initial treatment of the compound fracture of the right femur consisted of sulfadiazine by mouth and splinting of the extremity. The wound of entrance was at the trochanter of the femur. There was no wound of exit. The patient was transported overland and it was not until forty-eight hours after injury that débridement was done and a plaster hip spica was applied at a portable surgical hospital. On the fifth day after injury he was admitted to this hospital. The patient appeared to be greatly weakened. Temperature was 101° F. and pulse rate 96. Red blood cells were 2 million, hemoglobin 40 per cent, and white blood cells 20,000. A window was cut in the cast over the wound of the right subtrochanteric region. Dark brown, foul-smelling pus drained from the wound. Penicillin therapy was started at once. Because of the fever, the anemia, and the foul drainage, the cast was removed on February 23, the seventh day after injury. The soft tissues about the wound were indurated. Skeletal traction was instituted by means of a Kirschner wire through the upper tibia. In the next twelve hours there were three hemorrhages from the wound. The last of these was exsanguinating. This was controlled by clamping and suturing the bleeding points in the friable, dark red, granulation tissue which made up the floor of the wound. No packing was inserted; 2,000 c.c. of whole blood were given. The laboratory reported the recovery of *Bacillus subtilis* and *Cl. welchii* from cultures of the wound. Gas bubbles could be expressed from the floor of the wound. Because the patient's general condition was satisfactory, surgical intervention was withheld although penicillin therapy (50,000 units every three hours) was continued. An average of 400,000 units of penicillin was given intramuscularly each day from Feb. 22 until Feb. 25, 1945, when the patient suddenly became acutely ill. The temperature, which had not been over 101° F., rose to 104° F. The pulse rate rose suddenly from 92 to 120. Respirations increased from 20 to 40 per minute. The patient became apprehensive, restless, and thirsty. Crepitation of the tissues about the

wound, extending down the thigh to the toes and up to the iliac crest, had developed. The dorsalis pedis and posterior tibial pulses were palpable but faint. The entire thigh and the right lower abdominal quadrant were edematous and indurated. At emergency operation on February 25, nine days following injury and after three days of intensive penicillin therapy, the wound of previous débridement was enlarged upward to the crest of the ilium and downward to the knee. Gray-brown pus exuded from a cavity in and about the fractured fragments of the femur. Beyond this encapsulated area the rapidly spreading anaerobic infection manifested itself by discoloration and edema of the subcutaneous and areolar tissues and by multiple, small, elliptical areas of degenerated muscle, colored brown to black. These areas were limited to the vastus lateralis and the lateral portion of the quadriceps femoris. All involved muscle was excised. The temperature ranged from 101 to 103° F. for five days after operation. Therapy during this postoperative period included sulfadiazine (total of 78 Gm.), gas gangrene antitoxin (total of 200,000 units), blood transfusions, and penicillin. The latter was given by hourly intramuscular injection at the rate of 1,200,000 units daily. During the period from February 22 until March 8, at which time the patient was considered to have recovered, 5,800,000 units of penicillin were given. Gas gangrene antitoxin was discontinued after the fourth day of administration because of the development of severe urticaria. Cultures from the wound, taken before and after radical surgery, and while penicillin was being administered, were as follows: February 23, *B. subtilis*, *Cl. welchii*; February 24, *Proteus vulgaris*, pleomorphic streptococcus; March 2, *P. vulgaris*, *B. subtilis*; March 6, *Clostridium* of the proteolytic group; March 19, *Cl. welchii*. On April 25 split grafts were applied. The patient was sent to the United States. It is considered significant that the spreading clostridial myositis developed while the patient was receiving penicillin therapy.

There were six patients in whom there was *clostridial myositis* of all muscles of an extremity. These were patients in whom there was abrupt onset of signs and symptoms. Pain was severe; fever was high; leucocyte count was very high. The pathology was that of muscular necrosis spreading rapidly to involve all muscles of the extremity.

#### CLOSTRIDIAL MYOSITIS (GAS GANGRENE)

CASE 2.—A 22-year-old infantryman suffered a fracture of the fibula due to 0.30 caliber bullet. Débridement of the wounds of entry and exit was done within two hours. Incisions for débridement were not extensive. The patient was admitted here on the fourteenth day after injury with a bloodsoaked cast extending from toes to above the knee. On the morning after admission the cast was removed because the patient complained of severe pain. The tissues of the leg about the wounds were indurated and edematous. There was no crepitation. The dorsalis pedis and posterior tibial pulses were present. Temperature was 100° F., pulse 84, respirations 20. Red blood cells were 1.9 million, hemoglobin 40 per cent, and white blood cells 16,350. After four hours of observation during which the patient was treated with penicillin and blood transfusions the pulse rose to 140 and he showed signs of extreme toxicity. There was marked edema of the leg from the mid-thigh down. The skin of the leg was very pale and the dorsalis pedis and posterior tibial pulses were no longer palpable. White blood cells rose to 43,600. At the time of operation the wounds were enlarged by incision. All subcutaneous tissues were intensely edematous and pale. Incision of the fascial sheaths revealed that the musculature was intensely swollen, pale, and did not contract. Incision over the thigh revealed the same pathologic changes. High thigh amputation was done. Recovery was prompt.

These six patients had been treated by penicillin from the time of injury until the onset of the disease. In this group of cases the leucocytosis varied from 25,000 to 50,000. Anemia varied from 3 million to 3.5 million. Four patients recovered following amputation. Two patients developed severe toxemia and

died. There was distinct bronzing of the skin before death. The mortality rate in these fourteen cases of clostridial myositis was 21.4 per cent.

*Anaerobic Cellulitis.*—There were twenty-three cases in which the signs and symptoms were those of anaerobic cellulitis. This does not include cases of localized abscess from which pathogenic clostridia were recovered. These cases of cellulitis were characterized by gradual onset of diffuse edema of subcutaneous and areolar tissues. The muscles were not involved. The average lapse of time between injury and onset of the complication was fifteen days. The wounds of injury in these patients were as follows: fracture of the femur, 5; of tibia and fibula, 6; of the bones of the foot, 3; of the scapula, 1; wound of soft tissue of thigh, 4; of buttock, 2; of chest wall, 2. In sixteen of these patients débridement had been done within six hours after injury. In the other seven there was a lapse of twenty-four to seventy-two hours before operative treatment was given. All of these patients were pale, toxic, and febrile. They did not complain of pain. Secondary anemia was evidenced by the red blood count which varied from 2 million to 3.5 million cells with hemoglobin of 40 to 65 per cent. White blood count varied from 5,000 to 15,000. Temperatures were not high. The lowest recorded was 99.6° F. while the highest was 101.6° F. *Cl. welchii* was recovered from wound culture in all twenty-three cases. Penicillin had been given while the patients were en route to this hospital in eighteen cases. On admission their casts were stained with blood and pus and had a foul smell. The usual procedure was to remove the cast and to institute balanced traction. It was following the use of this necessary measure that these patients developed anaerobic cellulitis. The impression obtains that the motion of fascial planes coincident to removal of the plaster cast and the institution of traction opens up lymphatic channels and tissue spaces to allow for the extension of latent anaerobic infection. Commonly there was grayish slough in the depths of the wounds. Thick, dark brown or yellow pus with bubbles of gas could be expressed. There was no change in the skin or in the state of the circulation of the extremity. The extent of edema varied. In some patients it involved the entire extremity. Palpation revealed crepitation of tissue and there was abundant gas in the tissues as shown by x-ray. All of these patients were treated by radical incision and drainage. Five or six long vertical incisions were made through the involved areas and into neighboring healthy tissue. Subcutaneous and areolar tissues of the fascial planes were yellow green and edematous. Musculature was not abnormal. In some cases there were loose blood clots widely disseminated in the intermuscular areolar tissues. As an adjunct to surgery all patients were treated with penicillin. In seventeen cases the drug was given in doses of 300,000 units every three hours, intramuscularly. In six cases the same doses of penicillin were injected into healthy tissue proximal to the infected area. All patients in this group recovered. The role of penicillin in these cases will be discussed later. Case 3 is rather typical of anaerobic cellulitis due to *Cl. welchii* as observed in this group.

#### ANAEROBIC CELLULITIS

CASE 3.—A 22-year-old paratrooper sustained a compound fracture of the upper third of the femur from Japanese machine gun fire on March 13, 1945. Eight hours after injury he

arrived at an evacuation hospital in a state of shock. Débridement was done fourteen hours after injury. The wound of entrance was excised, the foreign body was removed, and the fascial sheaths were incised. A hip spica was applied. Penicillin (25,000 units every three hours) was started just after operation. It was continued until March 24, the date on which the patient was admitted to this hospital. The patient stated that he could not stand the "foul smell of the cast." He was apprehensive but not alert or restless. Temperature was 101° F., and pulse rate was 112. Red blood cells were 3.2 million, hemoglobin 70 per cent, and white blood cells, 12,000. X-ray showed malposition of the comminuted fracture. Blood transfusion was given, the cast was removed, and the extremity was suspended by skeletal, balanced traction. The entire thigh and leg were swollen and pale. Dorsalis pedis and posterior tibial pulses were palpable. There were three wounds, one over the lateral aspect of the thigh and two over the posterior thigh near the buttock. These were lined with dark brown, friable, granulation tissue, and thick brown pus and gas could be expressed. Smear from the wounds showed gram-positive rods. Wide incisions were made over the anterior, lateral, and posterior aspects of the thigh. In the floor of the wound, remnants of musculature of the vastus lateralis had sloughed but the main portion of that muscle belly was viable. Beyond that area, up to the iliac crest and down to the knee, the subcutaneous fat and the areolar tissues of the thigh were edematous and yellow green in color. Layers of liquefied and necrotic blood clot were evacuated from between the fascial planes of the thigh. Cultures from the wound were positive for *Cl. welchii*. Following operation the patient had temperature of 103 to 104° F. daily until the sixth postoperative day, when it dropped by lysis to normal. Penicillin (given at the rate of 50,000 units intramuscularly every three hours) apparently had no effect on the rate of recovery. Wound cultures failed to show *Cl. welchii* after the tenth postoperative day. Wounds were covered with split grafts fourteen days after incision and drainage. The patient made an uneventful convalescence from that time on.

Included in this group are five cases in which anaerobic cellulitis was superimposed on peripheral gangrene due to injury to the main arterial supply of an extremity. These were cases in which the artery had been ligated at the time of débridement of the wound. The patients were received at this hospital fourteen to twenty-one days after injury and gangrene of the digits was in evidence at that time. In three of the patients the brachial artery had been ligated. In a fourth the injury was a fracture of the femur complicated by laceration of the femoral artery. The fifth patient had fractures of both bones of the forearm with occlusion of the radial and ulnar arteries. The clinical picture in these cases was similar to that in the other cases of anaerobic cellulitis. Treatment was by amputation of the gangrenous digits, incision and drainage of the indurated, edematous tissues, and novocain block of the regional sympathetic ganglia.

#### HEMORRHAGE FROM THE WOUND

In the literature, attention has been called to the fact that hemorrhage from the wound may be the first sign of gas gangrene. This sign was present in six of the thirty-seven cases in this series. In three of these the hemorrhage was of minor importance while in three others it was severe and exsanguinating. Exploration at the time of operation showed a constant pattern in these patients. The hemorrhage was from the deeper recesses of a wound which was lined with friable, dark red or brown granulation tissues. Proximal ligation of the major artery was not effective in any of these cases. In five patients it was possible to control the hemorrhage by clamp and ligature of the bleeding points. In the

other three it was necessary to amputate the extensively damaged extremity. In two patients hemorrhage complicated abscess which had developed secondary to the position of the extremity in balanced traction following incision and drainage for anaerobic cellulitis. An example is the case of a soldier with a compound fracture of the upper third of the femur complicated by anaerobic cellulitis of the tissues of the thigh and buttock. Following radical incision and drainage his condition improved. However, the picture was complicated by the development of gangrenous cholecystitis. The patient again improved following cholecystectomy. Culture from the wound continued to be positive for *Cl. welchii*. During this time the extremity was in balanced traction and gravity favored the development of a localized infection high in the muscles of the upper gluteal area. The first evidence of complication was the sudden severe hemorrhage from the wound. Exploration revealed uncontrollable bleeding from the indurated granulation tissue of the deep recesses of the wound. Because of the critical condition of this greatly weakened patient and the extensive trauma to the bones and soft tissues of the leg, amputation was the only resource of the surgeon. The lesson to be learned from these cases is that if the culture for *Cl. welchii* does not become negative relatively soon following incision and drainage, further drainage or excision of necrotic tissue is indicated.

#### ADJUNCTS TO SURGERY

In the management of these cases of infection and gangrene due to *Cl. welchii* an attempt was made to determine the value of the chemotherapeutic agents. The use of sulfadiazine has been advised because of its bactericidal action against pyogenic organisms, the presence of which create wound conditions favorable for the growth of anaerobes. Because of the experimental evidence presented by McIntosh and Selbie<sup>2</sup> and by Hac<sup>3</sup> and others that penicillin is a potent therapeutic agent in gas bacillus infections, use of this drug as an adjunct to surgery has been advised strongly. Gas gangrene antitoxin has been recommended for prophylactic and therapeutic use. Analysis of the records of the thirty-one cases included in this report and the clinical impressions of the surgeons of the staff of this hospital are the basis for the opinions which follow. Sulfadiazine had been given in adequate amounts as a prophylactic agent to twenty-four of the thirty-seven patients who developed clostridial infection or gangrene. It was used after operation in the treatment of thirty of the thirty-seven patients. Its use produced no significant change in the flora of wounds. The general condition of patients did not improve following its use. There was no evidence that sulfadiazine was of value.

The fact that gas gangrene antitoxin had been given prophylactically in the forward areas to only nine of the thirty-seven patients indicates that surgeons are not convinced of its value. At this station the antitoxin was given therapeutically to eight patients. There was no obvious effect on the degree of toxemia. In five cases the use of the antitoxin was followed by the development of severe urticaria.

Effort was made to evaluate penicillin in the management of infections and gangrene due to *Cl. welchii*. Thirty of the thirty-seven patients included in this

report had been treated continuously with penicillin from the time of surgical débridement until arrival at this hospital. Penicillin had been administered intramuscularly in doses of 20,000 or 25,000 units every three or four hours. Experience with these thirty patients who developed clostridial infection or gangrene while penicillin therapy was in effect is convincing evidence that it has no prophylactic value. Following radical surgery, thirty-one of the thirty-seven patients were treated intensively with penicillin, 50,000 units being given intramuscularly every three hours for a minimum of ten days. In the other six patients the penicillin was injected circumferentially into the muscles of the extremity proximal to the infection. The administration of penicillin had no effect on the degree of toxicity, on the course of the fever, or upon the appearance of the wound. Surgeons who attended these patients are united in the opinion that penicillin has little or no value in the therapeutics of infections and gangrene due to *Cl. welchii*. In all cases clinical improvement was attributed directly to radical surgery. No other measure could substitute for the frequent transfusions of whole blood which were the mainstay of postoperative management.

*Differential Diagnosis.*—In Table III are listed the essential data in the cases reported. Fever and leukocytosis were higher in the case of clostridial myositis than in those of anaerobic cellulitis. Secondary anemia was present in all cases. Hemorrhage was a complication only in chronic anaerobic infections which had

TABLE III. DIFFERENTIAL CLINICAL AND LABORATORY DATA

	CLOSTRIDIAL MYOSITIS (14 CASES)	ANAEROBIC CELLULITIS (23 CASES)
Time from injury to onset	10 days	15 days
Penicillin therapy previous to onset	12 cases	18 cases
Débridement under six hours	12 cases	16 cases
Pain	Severe	None
Débridement not done	2 cases	0 cases
Toxemia	Severe	Mild
Fever	Usually 102° F. (may be as high as 104° F.)	99 to 101° F.
Anemia	R.B.C. 3 to 3.5 million	R.B.C. 2.2 to 2.9 million
Leukocytosis	W.B.C. 15,000 to 45,000	W.B.C. 5,000 to 15,000
Swelling	Marked swelling usually involving entire extremity	May involve all or any part of an extremity
Crepitation	Present in 6 cases, absent in 8 cases	Present in 17 cases, absent in 6 cases
Peripheral pulses	Normal in 6 cases, weak in 2 cases, absent in 6 cases	Present in all cases
Pathology	Loss of contractibility of muscles with palor and edema, patchy hemorrhagic necrosis, or brown discoloration of muscle groups	Edema and yellow-green coloration of subcutaneous and areolar tissue with or without gas bubbles; may be blood clots in fascial planes; muscles not altered
Gas	Variable	Abundant
Smell	May not be significant	Foul
Bacteriology	<i>Cl. welchii</i> all cases	<i>Cl. welchii</i> all cases
Surgery	Excision of muscles involved, 6 cases; amputation, 8 cases	Multiple wide incisions
Result	11 recovered, 3 died	All recovered

been incompletely drained. Pain was severe in the cases of clostridial myositis and absent in those of cellulitis. Surgeons of this hospital staff, observing large numbers of war wounded whose extremities were encased in plaster, soon learned that pallor, low grade fever, pain under the cast, and foul discharge from the wound suggested anaerobic infection and demanded removal of the cast and surgical intervention.

#### SUMMARY AND COMMENT

Report is made of experience with thirty-seven cases of anaerobic infection and gangrene occurring in war wounds. These cases were encountered in the management of 4,040 battle casualties from the campaign for the Philippine Islands. The patients were admitted to a general hospital five to twenty-one days after injury. There were fourteen cases of clostridial myositis and twenty-three cases of anaerobic cellulitis. The primary injury was compound fracture in 75 per cent of the patients and wound of soft tissue in 25 per cent. Pain, anemia, fever, and foul discharge from the wound are the signs which suggest to the clinician that a war injury may be complicated by anaerobic infection or gangrene. The opinion is advanced that incomplete débridement without dependent drainage is the most important factor contributing to the development of clostridial infection and gangrene in war wounds. Symptoms, signs, pathology, laboratory findings, and treatment are discussed. Illustrative case histories are reported. Experience with secondary hemorrhage is discussed. All the patients with anaerobic cellulitis recovered. Three of the fourteen with clostridial myositis died. The mortality rate in this group of cases is 21.4 per cent. Adjuncts to surgery are evaluated. Thirty of the thirty-seven patients included in this report were treated with large doses of penicillin from the time of initial débridement until the development of anaerobic infection or gangrene. All thirty-seven of these patients were treated intensively with penicillin after radical surgical treatment of the complication of anaerobic infection or gangrene. In six of these patients penicillin was injected intramuscularly just proximal to the infected area.

The evidence is convincing that penicillin is of no value in the prevention of clostridial infection or gangrene. Though the evidence is not sufficiently complete to warrant final conclusion, the opinion is held that penicillin is of no value in the therapeutics of these complications. The prevention of anaerobic cellulitis and gas gangrene depends upon early and adequate débridement of the wound with the establishment of counterdrainage. All evidence supports the conclusion that radical surgery is the method of choice for the treatment of anaerobic infection and gangrene in war wounds.

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## CAUSES OF AMPUTATIONS IN BATTLE CASUALTIES WITH EMPHASIS ON VASCULAR INJURIES

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IN CERTAIN quarters, particularly in the Zone of Interior in the United States, among men who have not seen battle casualties in the field, there seems to be an impression that many of the amputations performed in World War II could have been avoided. Various methods of therapy have been advocated to reduce the amputation rate. These include the application of sympathetic block, sympathectomy, and methods of vascular repair. In order to give a true picture of the problem of amputations I would like to present facts and figures from one of the armies which carried a major part of the fighting in Europe, and which incurred, in the course of this fighting, its share of battle casualties.

A detailed study of amputations was carried out in the Third U. S. Army through the cooperation of the Chiefs of Surgery and Surgical Team Chiefs with the Surgical Consultant. In no case was amputation done without consultation. All surgeons were made cognizant of the latest work on vascular repair. Conservatism was the watchword and was always emphasized. In fact, in retrospect I now feel that conservatism was to some extent overemphasized, as occasionally a life was lost in attempting to save a limb.

It is true that there are more amputees from World War II than from World War I. It is also true that there were far more casualties in the former, and that more wounded men have lived to return home without an arm or leg. The use of missiles that were more destructive is well known, and particularly affecting amputation was the extensive use of mines practically unknown in World War I. The direct results of mine injuries are shown in the differential of 1,375 cases of lower extremity amputations as compared with 458 of the upper extremity.

A breakdown of the level of amputations is shown in Table I.

The three main causes of amputations in World War II are shown in Table II. It is noteworthy that the fourth cause of amputations in World War I, secondary infection, has been eliminated by early adequate débridement and the chemotherapeutic agents, namely, penicillin and the sulfonamides. These drugs were given by mouth and parenterally, however, their local use in wounds was discouraged.

### GAS GANGRENE

During the nine months of this campaign, 445 patients with clostridial infection were encountered. Of this number, 258 came to amputation. In order to prevent unnecessary amputation, upon the first appearance of gas in the tissues, the clostridial infections were classified as follows:

1. Diffuse clostridial myositis in which amputation as far above the visible evidence of involvement as possible was performed immediately.

TABLE I. AMPUTATION LEVELS

LEVEL	NUMBER OF CASES
Upper arm	216
Forearm	188
Hand	54
Thigh	448
Leg	774
Foot	153
Total	1,833

TABLE II. CAUSES OF AMPUTATIONS

CAUSE	NUMBER OF CASES	PERCENTAGE
Gas gangrene	258	14
Blood vessel injuries	423	23
Traumatic	1152	63
Total	1,833	

2. Clostridial cellulitis involving only a muscle or group of muscles, in which wide incision of the localized process and excision of the devitalized tissue were sufficient and amputation was avoided.
3. Localized clostridial abscess in which incision and drainage were all that were necessary. Gas gangrene antitoxin was used in large doses in infections, but the general impression was that it was of very little value. Penicillin dosage was markedly increased in patients with clostridial infection, but it was felt that its sole value lay in controlling secondary infection, and that it had little effect upon the Welch bacillus.

Diffuse clostridial myositis accounted for 14 per cent of the total number of amputations. In this connection it is well to point out that in the wounded German soldiers handled by our hospitals the rate of clostridial myositis was four times as high as our own. The best explanation of this difference lies in the greater delay from time of injury to surgical care of these prisoners. It was often several days before they were evacuated to our hospitals. Once they arrived there, they received the same treatment as our own wounded men.

#### TRAUMATIC AMPUTATIONS

By far the greater number of patients seen in the military hospitals of this country, minus an extremity, lost that member immediately when hit, or it was so badly mangled that the damage was beyond repair. A typical lower extremity injured by an exploding German mine is shown in Fig. 1. This picture should be kept in mind by those enthusiasts who would "prevent 90 to 100 per cent of amputations by sympathetic block or sympathectomy," or "effect an over-all reduction of 50 per cent in limbs lost by blood vessel anastomosis."<sup>3, 4</sup> This group of cases accounted for 63 per cent of all the extremities amputated in this Army. Those who saw these patients in forward hospital units realized that no known surgical methods could have saved these limbs.

## VASCULAR INJURIES

In the group of vascular injuries the greatest salvage of extremities can be accomplished. This group borders on the traumatic group very closely in many cases, as these wounds were very often multiple, seldom a single laceration or puncture wound of a major artery, but when the surgeon felt that the injury to the blood supply was the paramount lesion the injury was classified as vascular. The group is much smaller than many surgeons suppose, as in 92,030 battle casualties there were only 837 such cases, or 0.9 per cent. Because of the fact that all surgeons had been alerted to be on the lookout for vascular injuries, and excellent records were kept, it is my impression that this figure is accurate. Of these 837 injuries to major arteries, 423 came to amputation and the main vessels involved are shown in Table III.



Fig. 1—Injury from German land mine.

The surgeons of this Army were thoroughly indoctrinated with the importance of attempting repair of major vascular injuries. Reports<sup>3, 4</sup> by Blake-more and his associates on the nonsuture repair of blood vessels, a very commendable work, were reproduced and a copy placed in the hands of every chief of surgery and surgical team chief.

The vitallium tubes and heparin necessary for application of their method were not available in large quantities, but there was sufficient material to give the method a fair trial.\* It was the consensus of opinion that some of the pro-

\*The vitallium tubes and heparin were made available for clinical trial to all Theater and Army Surgical Consultants through the efforts of the Chief Consultant in Surgery, Office of The Surgeon General.

TABLE III. BLOOD VESSEL INJURIES WHICH LED TO GANGRENE AND AMPUTATION

ARTERIES	NUMBER OF CASES
Subclavian	4
Axillary	18
Brachial	80
Cubital	2
Radial	2
Ulnar	1
Radial and ulnar	3
Common iliac	6
External iliac	7
Femoral	104
Popliteal	157
Anterior tibial	3
Posterior tibial	16
Anterior and posterior tibial	20
Total	423

cedures advocated by Blakemore and associates are impractical for use in the field.<sup>3, 4</sup> These include the following points: (1) The recognition of injury to a major vessel by an aid man on the battlefield is impossible. The therapy cannot be instituted by him. The limitations of such a man, or the conditions under which he works, have not been taken into consideration in making such a recommendation. (2) The institution of surgical procedure in the battalion aid station, where only resuscitation has been practiced, would require the revision of the entire system of handling casualties in forward areas. Such might be advocated if there was a large enough number of vascular injuries, but not when these cases constitute less than 1 per cent of the total number of casualties. (3) The time interval between wounding and the institution of surgery has been misunderstood. This interval has been greatly reduced in World War II over World War I, but still ranges between six and twelve hours, even in emergencies. The average case was usually disposed of surgically under twenty-four hours, and surgical staffs worked long hours to accomplish this result. (4) The preparation of fresh vein grafts was time consuming and had frozen grafts been available another objection would have been removed. However, I do feel, as most of the surgeons in our Army, that this work is a step in the right direction and the method was successfully applied in selected cases.

In lieu of the Blakemore apparatus, glass tubing and plastic tubing were used in a few cases. In all of these nonsuture methods of blood vessel anastomosis it is essential to use heparin,<sup>5, 6</sup> to prevent clotting at the site of repair. The use of heparin in battle casualties is a procedure coupled with considerable risk, as at least one-third of all casualties have multiple wounds and fatal hemorrhage has occurred in a number of heparinized patients.

The treatment used and the results in the cases in this series are shown in Table IV. From this table it would appear that the Blakemore method of vein graft has a slight advantage, but that on the whole about 50 per cent of the patients developed gangrene no matter what method of treatment was used. This is not in fact true, and it is necessary to break down these figures into the vessels involved, as well as the treatment used, in order to draw any comparison.

TABLE IV. TREATMENT OF 837 MAJOR BLOOD VESSEL INJURIES

METHOD	NUMBER	RESULTS		PER CENT DEVELOPED GANGRENE
		GANGRENE	VIALE	
Ligature	767	386	381	50
Suture	42	23	19	51
Nonsuture	28	14	14	50
Blakemore	15	7	8	46
Glass tubing	9	5	4	55
Plastic tubing	4	2	2	50
Total	837	423	414	50.5

TABLE V. INJURED VESSELS TREATED BY LIGATION

ARTERY	NUMBER	VIALE	GANGRENE	PER CENT DEVELOPED
				GANGRENE
Subclavian	9	5	4	44
Axillary	29	15	14	48
Brachial (above profunda)	69	32	37	55
Brachial (below profunda)	141	108	33	23
Cubital	4	2	2	50
Radial	25	23	2	8
Ulnar	22	21	1	4.5
Radial and ulnar	8	5	3	37
Common iliac	6	1	5	83
External iliac	6	2	4	66
Femoral (above profunda)	74	12	62	84
Femoral (below profunda)	62	27	35	56
Popliteal	196	51	145	74
Anterior tibial	21	18	3	13
Posterior tibial	69	53	16	23
Anterior and posterior tibial	26	6	20	76
Total	767	381	386	50

In Table V are shown the results in the vessels treated by simple ligation.

In order to emphasize the marked difference between the problems encountered in the surgical care of vascular injuries in battle casualties and those met in comparable injuries in civilian practice, Table VI is produced.

These marked variations in results are not due to a difference in treatment. The therapy recommended by the council was adhered to in regard to simultaneous division of the companion vein, and the routine use of sympathetic

TABLE VI. SUDDEN ARTERIAL LIGATION AND GANGRENE

ARTERY LIGATED	PER CENT DEVELOPED GANGRENE (BATTLE CASUALTIES)	N.E.C. CHART (PER CENT)*
Subclavian	44	9
Axillary	48	9
Brachial	55	3
Cubital	50	0
Common iliac	83	50
External iliac	66	13
Common femoral (above profunda)	84	21
Femoral (below profunda)	56	10
Popliteal	74	0
Anterior tibial	13	3
Posterior tibial	23	3

\*Figures in this column from Military Surgical Manual.<sup>2</sup>

blocks both before and after surgery. A major part of the difference, it is felt, can be found in the fact that the battle casualty has had the injury for from six to twelve hours before he reaches a surgical unit. He is often exsanguinated, has a low blood pressure, and is in shock. His tissues are anoxic. There is often hemorrhage into the fascial planes of the extremity with a resulting hematoma and pressure on the collateral circulation. Often the collateral circulation has been injured also. The disappointing results from sympathetic blocks are accounted for, in a large part, by these latter facts rather than that the blocks were not well done.

In Table VII are shown the results in the seventy vessels that were repaired. Repair by suture remains the method of choice whenever applicable even if it means reduction of the caliber of the vessel by as much as 50 per cent.

TABLE VII. INJURED VESSELS TREATED BY REPAIR

ARTERY	SUTURE	DEVELOPED GANGRENE	NONSUTURE	DEVELOPED GANGRENE
Subclavian	1	0	0	0
Axillary	5	2	3	2
Brachial (above profunda)	9	6	3	2
Brachial (below profunda)	6	2	4	0
Cubital	0	0	0	0
Radial	0	0	0	0
Ulnar	0	0	0	0
Radial and ulnar	0	0	0	0
Common iliac	2	1	1	0
External iliac	2	2	2	1
Femoral (above profunda)	6	4	3	2
Femoral (below profunda)	4	1	2	0
Popliteal	7	5	10	7
Anterior tibial	0	0	0	0
Posterior tibial	0	0	0	0
Anterior and posterior tibial	0	0	0	0
Total	42	23	28	14

It will be noted readily that only the larger arteries, including subclavian, axillary, brachial, iliac, femoral, and popliteal, were repaired, so in order to draw a fair comparison, only the same arteries should be considered from the group treated by ligation. In Table VIII this comparison is shown.

TABLE VIII

MAIN ARTERIES	NUMBER	GANGRENE	VIALE	PER CENT DEVELOPED GANGRENE
Ligature	592	339	253	57
Repair	70	27	43	38

From these figures it is readily seen that where the major vessel was ligated, 57 per cent of the extremities involved developed gangrene, but where repair was the method of choice only 38 per cent developed gangrene. Thus, there is an advantage of 19 per cent of repair over ligation.

This conclusion cannot be too firmly drawn, however, because the repair series is much smaller and the more favorable cases were selected for repair. However, it is felt that there is an indication of distinct advantage where repair

is used, and it should be encouraged so that eventually better and more practical methods of vascular surgery will be evolved.

It will be noted that in this series there is no mention of arteriovenous aneurysm or false aneurysm. These patients were all treated conservatively in the forward areas and evacuated to the general hospitals in the rear. Operation is seldom undertaken in the patients for six weeks or more, and in the interval the collateral circulation is developed and gangrene of the extremity seldom results.

#### SUMMARY

A series of 1,833 amputations performed in the Third U. S. Army during the European campaign is reviewed. The levels of amputation are given. The causes of these amputations are reviewed with special emphasis on 837 vascular injuries. The results of arterial repair in seventy patients are shown. The percentage of extremities which became gangrenous following ligation at various levels of the main arterial supply is reviewed. These results are compared with the results in civilian practice and some of the probable reasons for these differences are stressed.

#### CONCLUSIONS

1. Traumatic amputation, gas gangrene, and vascular injury were the three main causes of the loss of limbs in World War II.

2. The extensive use of mines by the Germans caused an increase in the number of amputations, particularly those of the lower extremity.

3. Vascular injuries constituted less than 1 per cent of the total number of battle casualties.

4. Vascular surgery in battle casualties has made very little progress since World War I.

5. The method of Blakemore and associates of arterial repair by vein graft is a step in the right direction, but in general was not found to be practical for routine use in battle casualties with vascular injuries.

6. Sympathetic blocks were routinely used in casualties with vascular injuries, but the results were disappointing.

7. The repair of injured arteries produced 19 per cent less gangrenous extremities than ligation of the same group of vessels.

8. Continued emphasis should be placed on vascular surgery, in order to bring this field abreast of other surgical specialties.

All of the statistical data in this report were compiled through the cooperation of the Chiefs of Surgery and their staffs of the Evacuation Hospitals, and the Surgical Team Chiefs working in the Field Hospitals of the Third U. S. Army during the European Campaign from Aug. 1, 1944, through May 8, 1945. Because of their tireless efforts this report has been made possible. Many of the conclusions expressed in this paper are a consensus of the opinions of this splendid group of young surgeons who made one of the best records in the care of battle casualties yet produced by any army. They treated 92,030 battle casualties in nine months, with only 2,574 deaths, or a mortality rate of 2.76 per cent.

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## A COMBINATION ARM SPLINT AND NEEDLE-HOLDER DEVICE

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THE present method of fixation of intravenous needles by tying the arm on a board splint and taping the needle leaves much to be desired from both technical and physiologic considerations. The development of a practical method of fixation of intravenous needles, allowing the patient some movement of the arm as well as affording a more stable placement of the needle and a wider choice of arm veins, would be a boon to both the intern and the nurse. With these objectives in mind we began the development of a combination arm splint and intravenous needle-holder device. The result has been the construction of an instrument which circumvents most of the attendant difficulties and inconveniences of the past methods by achieving the objectives mentioned.

The specific difficulties which are encountered with the present method of intravenous fluid administration are:

1. The arm must be tied to a board very loosely if occlusion of the superficial venous return is to be avoided. This allows the restless or irrational patient opportunity for considerable movement of the arm and often results in displacement of the needle from the vein.
2. Any angular vein which is so placed that a major portion of the adaptor would not lie over the arm obviously cannot be used.
3. Tape often does not adhere well in cases of hirsutism, of arms which are wet (perspiration, fluid from the needle, alcohol), and of redundant skin (looseness of skin due to dehydration and weight loss).
4. The use of gauze in obtaining proper angulation of the needle often results in needle displacement.

The result of these many factors is that displacement of needles from veins in the course of continuous drip therapy is a commonplace event, and the almost constant attendance of a nurse to these patients is practically a necessity. This is especially true for those patients who are restless and irrational.

To be thoroughly practical, an instrument such as we are describing must not only obviate the undesirable features mentioned, but must also fulfill the following criteria: It must be (1) simply operated, (2) time-saving, (3) reliable, (4) constructible for general use at a reasonable cost, (5) comfortable and yet splint the arm satisfactorily, (6) light, compact, and easily cleaned.

The combination splint and needle holder which we are describing has successfully fulfilled these demands.

### DESCRIPTION

The instrument (Fig. 1) which we are describing embodies the following features:

1. A semicylindrical splint into which the arm is laid.

2. Four upright ratches, one at each corner of the splint.
3. Two crossbars adjustable on, and removable from, the upright posts at either end. (The crossbars are locked on the posts by a simple spring lock mechanism. Each crossbar is actually a tube from either end of

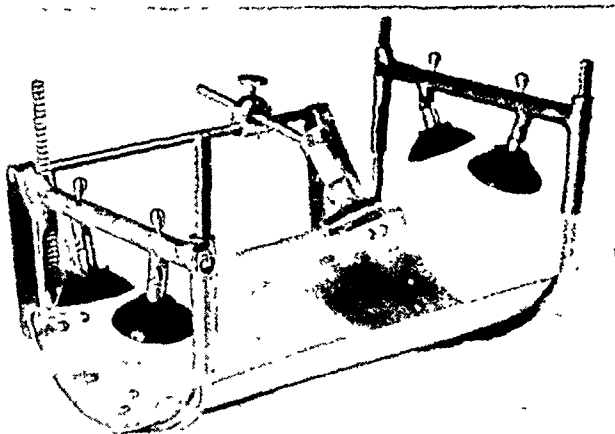


Fig. 1.—The combination arm splint and needle-holder device for the administration of intravenous fluids.

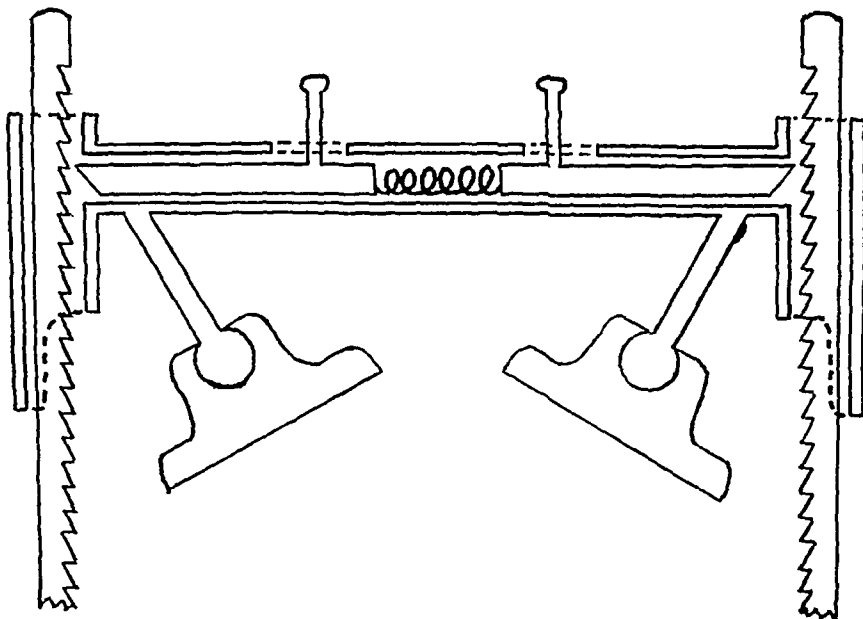


Fig. 2.—A drawing showing the mechanism of the crossbar mounted on the ratches.

which projects a pawl which fits into any interdentate space on the upright post. The detents are forced into position of engagement by a coil spring placed between them within the tube, as shown in Fig. 2. They are released by two triggers on the superior aspect of the crossbars. The crossbars readily slide down the upright posts to the desired

height, but they can be pulled upward only when the pawls are disengaged from the teeth by pulling the triggers together.)

4. Two legs extending downward from each crossbar on to each of which is mounted a circular rubber pad by means of a ball-and-socket joint.

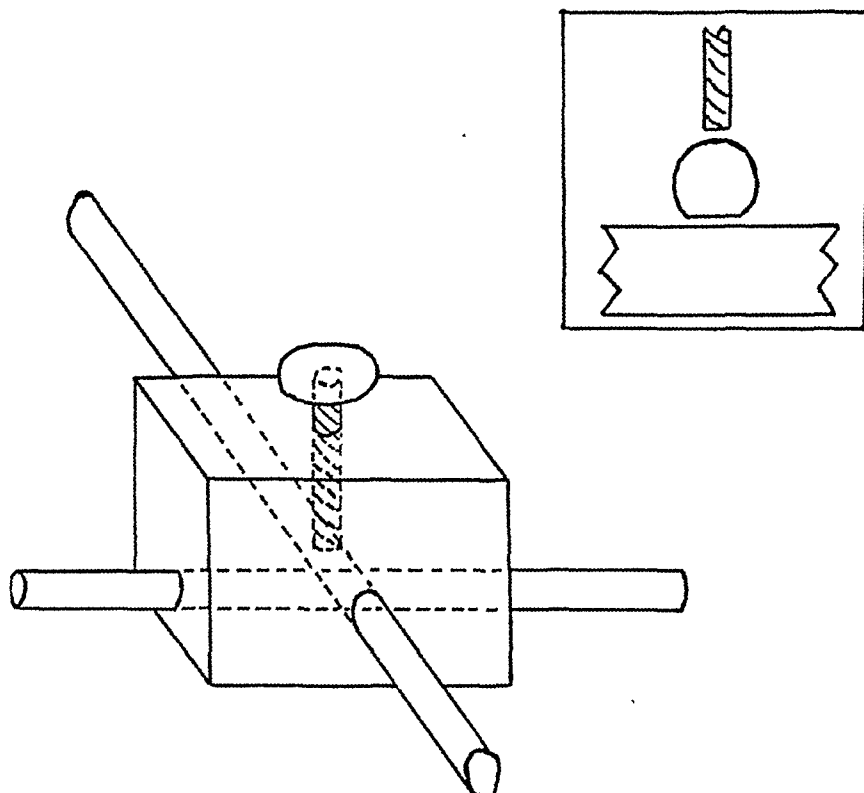


Fig. 3.—A drawing showing the method by which the transverse bar is locked in position. The inset shows the relations of the longitudinal bar, the transverse bar, and the lock screw within the housing.

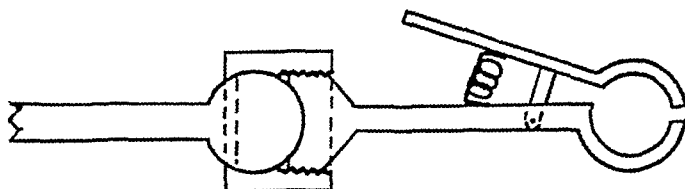


Fig. 4.—A drawing showing the mechanism of the spring clip needle holder and the universal joint which is locked by the threaded collar.

5. A round bar fixed to and running the length of the splint. (The bar is positioned lateral to and superior to the splint.)
6. A transverse bar running through a housing mounted on the longitudinal bar, as shown in Fig. 3. (By virtue of this arrangement the transverse bar may be fixed at any position to the long axis of the splint. In addition, the transverse bar slides medially or laterally through the housing, permitting fixation of the needle holder at any position in

relation to the short axis of the splint. All motion, both transverse and longitudinal of the transverse bar and the housing on the longitudinal bar, is stopped by the turn of a single phlanged screw.)

7. A spring clip needle holder attached to the medial end of the transverse bar by a universal (ball-and-socket) joint, as shown in Fig. 4. (This ball-and-socket joint is simply locked at any desired position by a turn of the screw mechanism of the collar.)

#### EXPERIENCE

We have used this apparatus on sixty-two patients over a period of three months at the Asbury Hospital in Minneapolis, Minn. It has been used on patients under varying conditions ranging from states of complete anesthesia to marked restlessness and irrationality. We have further found this instrument of inestimable value in bloodletting.

#### ADVANTAGES

Our experience has proved beyond question that the following advantages are enjoyed through use of this instrument.

1. This apparatus permits a speed of performance not attainable with the past method of tying and taping.

2. This method permits a firm and reliable splinting of the arm without embarrassing the venous return, because the rubber pads cover only a small surface area. The only satisfactory method of obtaining complete immobilization at present is to tape the arm to a splint. It need hardly be pointed out that this method is an expensive, time-consuming, and difficult feat. This second advantage pertains especially to restless and irrational patients.

3. Use of this device permits a certain amount of movement of the patient's arm (at the shoulder joint or at the elbow if the splint is applied to the forearm) without the needle pulling out of the vein or penetrating the distal vein wall.

4. The usual complications incident to intravenous therapy have been almost entirely obviated. In our series of sixty-two patients there was not a single instance in which hematomas or venous thrombosis occurred. Escape of fluid into the tissues occurred in two cases.

5. The appliance entirely avoids the inconvenience of using adhesive tape.

6. This combination splint and needle holder has proved to be invaluable in moving patients to and from the operating table when continuous intravenous fluid administration is desired.

7. The apparatus has proved to be extremely useful in phlebotomy. By use of a number of such instruments it would be a simple matter for one intern to be in charge of several simultaneous bloodlettings.

8. The patients have indicated their preference for this method of receiving intravenous fluid over the old method of tying and taping because of the comfort and security it affords.

9. The cleaning of this instrument is a simple matter; blood or fluid stains may be sponged off without difficulty.

10. This appliance permits the utilization of veins which are so located that the major portion of the needle adapter does not lie over the arm. In these instances it is impossible to tape the needle into place with any degree of security (see Figs. 5 and 6).

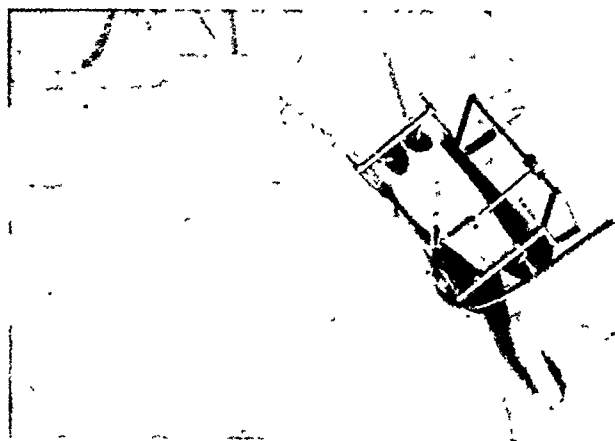


Fig. 5.—The instrument is here applied to the forearm with the needle in a vein so angulated that taping is not practical. (Application of the device to the patient's forearm permits movement at the elbow.)



Fig. 6.—Application of the apparatus in this manner completely immobilizes the elbow. Notice that in this case the needle is in a vein so angulated that the major portion of the adapter does not overlie the arm.

#### LIMITATIONS OF THIS COMBINATION SPLINT AND NEEDLE HOLDER

1. In the present construction the use of hand veins is difficult and frequently impossible. We believe we have found a practical solution to meet this shortcoming but have not incorporated this new feature into the present model.

2. The splint is not inclined to permit a moderate flexion of the forearm which would allow an optimum relaxation of the arm musculature. Incorporation of this feature would be a desirable improvement.

poration of such a feature would interfere seriously with the present versatility of this instrument in that the number of available positions of the splint on the arm would be significantly decreased. We have found that folding a towel and placing it at the distal end of the splint gives a practical solution in those cases where an inclination is desired.

3. It is not practical to use this splint at the junction of the foot and leg when use of the great saphenous vein is desired. This site, of course, is a relatively easy one for taping because of the normally small amount of movement at this location in a bedridden patient.

We wish to express our appreciation to Dr. C. J. Watson, professor of medicine, and Dr. O. H. Wangenstein, professor of surgery, at the University of Minnesota, and the Asbury Hospital Staff for encouraging us in this undertaking. We also wish to thank Mr. William Sielert for assisting us in building this instrument.

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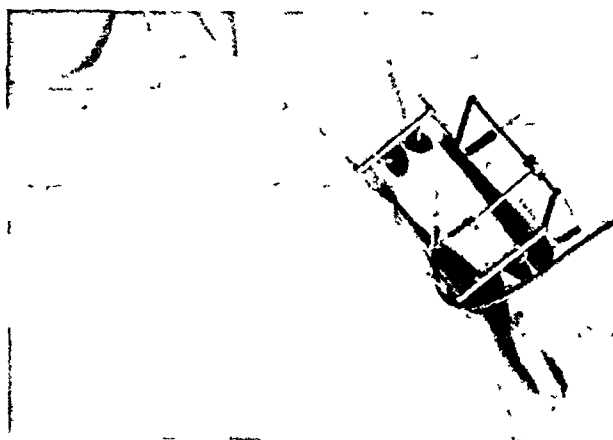


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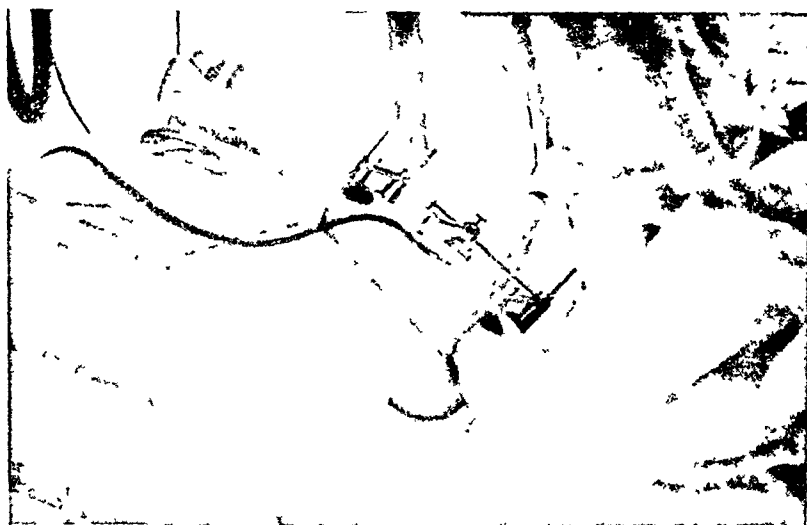


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Walter Edward Dandy  
(1886-1946)

# SURGERY

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## Dr. Walter E. Dandy Birthday Number

WALTER EDWARD DANDY

1886-1946

WALTER EDWARD DANDY died on Friday morning, April 19, 1946. The original suggestion that this issue of SURGERY be dedicated to him on the occasion of his sixtieth birthday came from friends in Australia. This suggestion met with the hearty approval of the editors of SURGERY. It was hoped that this series of papers would be published in April since Dr. Dandy's birthday was on the sixth of this month but several factors led to delay. In the meantime the untimely death of this great man has shocked the medical profession and thousands of his patients and friends.

Walter Edward Dandy, the son of John and Rachel Dandy, was born in Sedalia, Mo. He received a Bachelor of Arts degree at the University of Missouri in 1907 and was graduated from the Johns Hopkins School of Medicine in 1910. He served as a house officer in surgery at the Johns Hopkins Hospital during the succeeding eight years, the last two of which he was resident surgeon. In this capacity he followed Dr. Roy D. McClure and Dr. George Heuer and preceded the late Dr. Mont Reid.

The busy years as a house officer sharpened rather than dulled Dr. Dandy's interest in investigative work. Dr. Halsted recognized his unusual gifts and encouraged and stimulated him. In 1913, three years after his graduation, Dr. Dandy reported his fundamental studies on hydrocephalus, which added much to the knowledge of the pathogenesis and the treatment of this disorder. Dr. Halsted remarked to Dr. E. A. Park at the time, "Dandy will never do anything equal to this again. Few men make more than one great contribution to medicine." Subsequent events showed that Dr. Halsted had underrated the ability of his brilliant pupil.

In 1918, at the age of 32 years, Dr. Dandy made his greatest contribution. While viewing the x-ray film of the abdomen of a patient, he observed the difference in the appearance of shadows which were cast by air and by fluid. It occurred to him that the outline of the ventricles of the brain could be visualized if some of the fluid were removed and replaced by air. The pro-

cedure was used first on animals and later on patients. It was found that an abnormality in contour of one of the ventricles of the brain as seen on the x-ray film frequently revealed the location of lesions which could not be determined by other means. At first this method was not received with enthusiasm by most neurosurgeons, but it is used now in all medical centers and is regarded by many as the greatest advance ever made in neurosurgery.

Dr. Dandy's original work did not cease with this second contribution. In 1925 he described an operation for trigeminal neuralgia which reduced the likelihood of postoperative corneal anesthesia and ulcers. Shortly thereafter he developed a similar operative procedure for the treatment of glossopharyngeal neuralgia. In 1928 Dr. Dandy devised an operation for the treatment of Ménière's disease, which is regarded by many as his second most important contribution. He discovered that the attacks of vertigo could be eliminated by division of fibers of the anterior part of the acoustic nerve and that hearing was not impaired. No satisfactory treatment for this condition existed prior to this discovery.

In 1928 Dr. Dandy described the findings, together with the operative treatment, in several patients with ruptured intervertebral discs. He did not, however, appreciate the surgical significance of this disorder until the important work of Barr and Mixter was published. Following this he took a renewed interest in the subject and demonstrated the frequency with which a ruptured disc causes pain in the lower back and leg. New diagnostic tests were devised and operative therapy was improved.

Other achievements of Dr. Dandy's include the operative treatment of intracranial aneurysms, a field in which he alone achieved much success for a number of years. His operations for tumors of the acoustic nerves and for large lesions of the frontal lobes are almost equally outstanding. His book on the treatment of orbital tumors is a classic. At the time of the onset of his recent illness he was engaged in experimental and clinical studies on the so-called "conscious" center. It may be said truly that his interest and enthusiasm never waned and his imagination and genius led him from one discovery to another. Dr. Halsted once said to Dr. Abraham Flexner and to others that he regarded Dr. Dandy as the most brilliant pupil he ever had.

Despite his busy professional life, Dr. Dandy found time to play golf and tennis and his interest in sports in general was keen. He took great pride in a helmet which he devised for protecting the heads of baseball players. He was fond of bridge and was a good though somewhat unorthodox player. Dr. Dandy read extensively and was an authority on the history of the Civil War period.

An unusually happy home life was Dr. Dandy's greatest source of pleasure. The congenial life there meant more to him than any outside attractions, and it was very seldom that he could be induced to leave his home and family in the evening. He kept constantly in touch with the interests of his wife and children. Walter Jr. is a third year student at the Johns Hopkins Medical School, Mary Ellen a freshman at Wellesley, and Kitty Lou and Margaret

attend private schools in Baltimore. The interesting conversations and the pleasant give and take between parents and children were delightful. .

Many knew of Dr. Dandy's eminence as a neurosurgeon; few were acquainted with his generosity and his deep interest in students and associates. The cold exterior which a neurosurgeon of the formative days of this specialty had to assume if he were to continue in the discouraging work was only superficial. The student in need was aided in paying his tuition, the sick house officer or nurse was sent to a resort for a vacation, the orderly was given a home, the surgical department received an anonymous gift. Only the recipients knew of these acts of kindness and generosity.

Dr. Dandy possessed a fortunate combination of qualities: character, a clear-thinking brain, industry, an intuitive imagination, independence of thought and action, fearlessness and daring, manual dexterity, and a colorful personality. In a recent editorial in the *Baltimore Evening Sun* it was said, "He had imaginative genius to conceive of new and startling operative techniques, courage to try them, and skill—superb skill—to make them successful." It can be said without fear of contradiction that Medicine has lost one of its greatest men.

—Alfred Blalock

## AN APPRECIATION

WALTER DANDY'S achievements in the field of neurosurgery are epitomized in this issue of SURGERY by his associates and former pupils on his sixtieth birthday. It would be of the utmost value both to neurosurgeons and to those whose plan it is to enter this field were Doctor Dandy's articles, monographs, and books to be compiled into a complete set of volumes. These contributions are truly monumental.

As one of Professor Halsted's residents Doctor Dandy was well trained as a general surgeon, and was introduced early into the surgical research laboratory. This background has contributed greatly to his eminence as an investigator, teacher, and neurosurgeon.

One of his earliest and most unique and significant contributions to neurosurgery is the procedure of ventriculography and encephalography. It was conceived when he, as resident surgeon, noted the presence of air beneath the diaphragm in a roentgenogram of a typhoid patient with perforation. The contrast medium of this air suggested to him its use in replacing cerebrospinal fluid to outline the ventricles and subarachnoid spaces.

His early and sustained interest in hydrocephalus is again shown in a recent article. He has advanced the technique of approach to lesions of the cranial nerves, acoustic neuromas, and third ventricle and other tumors. These are detailed in his comprehensive chapter on the brain found in *Lewis' Practice of Surgery*.

I am primarily interested in calling attention to Doctor Dandy's prestige as a teacher. In exacting integrity, alert cerebration, and paramount interest in the welfare of each patient, he gave in return a share in the diagnostic, operative, and postoperative care of the patient, dependent only upon the ability of his assistant. Not content with existing procedures when these seemed to be inadequate, his keen observation and deduction often led to a solution which meant the saving of a life in an apparently hopeless situation.

His outstanding success in the accurate localization of brain lesions was in each case due to a most careful consideration of the clinical and neurologic findings, with comparative study of the ventriculograms, which had in some cases been repeated once or even twice.

Sustained investigative interest in the research laboratory, complete honesty in the interpretation of experimental findings, precise clinical diagnosis, and analysis of pre- and postoperative procedures—these precepts imply certain responsibilities for the training of others, and appreciation that can never be fully expressed.

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## EVOLUTION OF NEUROSURGERY THROUGH WALTER E. DANDY'S WORK

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"WHEN I was Dr. Cushing's resident, during the years 1911 and 1912, two intracranial tumors were removed, one survived." This fact, told by Walter Dandy to his pupils in a lecture delivered this year, gives an idea of the situation of neurosurgery of that time. At that period in the development of the surgery the localization of brain tumors was largely guesswork, and most tumors were found by trial and error, with only occasional successes. The usual procedures were explorations and decompressions to relieve intracranial pressure. It was hoped that eventually localization would appear before the patient's death.

Dr. Dandy's discovery of ventriculography made it possible to diagnose accurately nearly all tumors and, when present, to localize them with precision. Exploratory cranial operations were no longer justified, decompressions were eliminated, and exposures of brain tumors were made with accuracy because their location was known beforehand.

From 1910 to 1917, among Dandy's different works we have the series of brilliant and thorough experimental, pathologic, and clinical studies of hydrocephalus. Before his discovery of the cause of hydrocephalus, it was described in all textbooks as an idiopathic disease, and therefore no reasonable therapy was used. Dandy's experiments on animals by placing an obstruction in the aqueduct of Sylvius, foramen of Monro, or cisterna, reproduced every type of hydrocephalus. He discovered the place and manner of formation and absorption of cerebrospinal fluid. He finally checked the experimental studies by pathologic studies on human material. As a result, hydrocephalus has been emancipated from the diminishing group of so-called idiopathic diseases. Dandy's fundamental statements were as follows:

1. Fluid forms in the cerebral ventricles from the choroid plexuses but is not absorbed there.

2. Fluid is absorbed from the entire subarachnoid space over the cerebral and cerebellar hemispheres and spinal cord; the major part of the absorption is over the cerebral hemispheres. Absorption is directly and solely into the blood by way of the capillaries of the pia arachnoid, it is not through the pachianian granulations or stomata as taught in most textbooks of anatomy and physiology.

3. There must, therefore, be free escape of fluids from the ventricles into the cisterna magna and into the subarachnoid spaces over the cerebral hemispheres. If an obstruction exists at any point between the place of formation and place of absorption of fluids, the cerebrospinal fluid will continue to accumulate up to the point of the obstruction, hydrocephalus therefore resulting.

4. Clinical test: In order to know whether the obstruction is in the ventricles or subarachnoid space, an inert colored solution such as phenolsulfonphthalein is injected into the spinal canal and later tested for in the fluid of the lateral ventricles. If the dye does not come through, the block is in the ventricular system; if it does come through, the block is in the cisternae.

5. The three operations which were devised were based on this accurate anatomic, physiologic, and clinical knowledge: (a) Third ventriculostomy (floor of ventricle) to be used for obstruction at the aqueduct of Sylvius. (b) Reconstruction of new foramen at fourth ventricle when the foramina of Luschka and Magendie are occluded. (c) The bilateral removal of the choroid plexuses from the lateral ventricles when hydrocephalus is due to a cisternal block, and later, if necessary, cauterization of choroid plexuses in foramina of Luschka and Magendie.

*Diagnosis and Treatment of Strictures at the Aqueduct of Sylvius (the Iter).*—In July, 1945, Dandy published his work "Diagnosis and Treatment of Strictures of the Aqueduct of Sylvius (Causing Hydrocephalus)." In this work he gave the results of his experiences of nearly twenty-five years in this group of hydrocephalies.

In 1922, Dandy proposed an anterior third ventriculostomy in the floor of the ventricle through a small supraorbital approach.

In 1932, he substituted a lateral approach to the third ventricle by the temporal route and this has since been used exclusively.

Dandy demonstrated that structures of the aqueduct of Sylvius are diagnosed in infants and children by (1) the dye test indicating an obstruction, plus (2) a low inion, and (3) usually without ventriculography.

In his recent work Dandy made the following fundamental statements: (1) An oversized head with MacEwen's sign (cracked pot sound) and (2) an inion normally placed or at times lower than normal indicates that the hydrocephalus is due to a stricture of the iter. (3) If the inion is higher than normal under the same conditions, the obstruction is at the foramina of Luschka and Magendie (because the enlarged fourth ventricle, or tumor, pushes the inion upward).

Third ventriculostomy, or temporal approach, is the operative choice for hydrocephalus due to a stricture of the aqueduct. It is much superior to the anterior approach because (1) external hydrocephalus does not follow; (2) it is not necessary to section the optic nerve; (3) the scar is under the hairline.

Cures are attained in most cases when the patient is more than 1 year old and in less than one-half the cases of infants.

Excellent results were obtained in twenty-nine cases (patients over 1 year of age). From this group twenty-four are still living and cured. The time since operation is between six months and one year in two cases; between five and eleven years in eleven cases; and, finally, between ten and twenty-three years in four cases.

*The Treatment of Obstructions of the Foramina of Magendie and Luschka.*—In 1921, Dandy published "The Diagnosis and Treatment of Hydrocephalus Due

to Occlusions of the Foramina of Magendie and Lushka." In this work, Dandy described a group of cases of hydrocephalus caused by closure of the foramina of Lushka and Magendie, showing the pathology by post-mortem specimens, describing the means by which it can be diagnosed clinically, and introducing his operative procedure to produce its cure.

Dandy stated that there are two types of occlusions of the foramina of Lushka and Magendie: One, which occurs congenitally, may or may not be the result of an intrauterine inflammation; the second, which occurs at all ages, always follows some form of meningitis.

Dandy demonstrated from post-mortem examinations that the closure of the foramina of Lushka and Magendie in the same brain will, without exception, result in hydrocephalus because there are no collateral channels by which the fluid can be carried from the ventricles to the subarachnoid spaces.

*Ventriculography.*—Although each of Dandy's work establishes a landmark in the history of neurosurgery, his discovery of the ventriculography in 1918 started a new epoch, not only from the technical point of view but from the intellectual, since it transformed radically and integrally the mental conception of neurosurgery, replacing the existing dogmatism and empiricism with a realistic judgment and authentic scientific criterion.

It was in the same year, 1918, that the most prominent Argentine surgeon, Dr. Ricardo Finochietto, visited Dr. Dandy, seeing him perform in one day five operations, using in each a technique that he had devised. On that date began the cordial friendship between the two masters, to be so profitable later for the progress of Argentine neurosurgery, through their pupils. Through this friendship I became one of Dr. Dandy's pupils.

In 1920 Dandy published his work, "Localization or Elimination of Cerebral Tumors by Ventriculography." In this he made the following statements:

"Ventriculography is invaluable in the localization of obscure brain tumors. So-called unlocalizable tumors comprise at present over half of the total number."

"Practically all brain tumors either directly or indirectly affect some part of the ventricular system."

"Local changes in the size, shape, and position of one or both ventricles as shown by the ventriculogram will accurately localize most obscure tumors of either cerebral hemisphere."

"Every effort should be made to localize the tumors before resorting to any operative procedures."

"The usual subtemporal decompression is useless and dangerous when a hydrocephalus is present, i.e., when the tumor is in the brain stem or cerebellum."

"A suboccipital decompression (cerebellar operation) is extremely dangerous when the lesion is in the cerebral hemisphere."

"To differentiate between cerebral and cerebellar lesions is frequently one of the most difficult tasks in intracranial localization. Ventriculography at once separates these two groups and indicates the operation of choice."



In later works Dr. Dandy propounded the following fundamentals of modern surgery of the brain:

"Brain tumors are among the most frequent neoplastic lesions in the body; their growth is always progressive and almost always leads to a train of terrible sequelae and eventually to death."

"There is only one form of treatment of tumors of the brain, operative removal, and this must be complete."

"To obtain the best operative results, brain tumors must be diagnosed and localized in the earliest stages."

"It is now possible to diagnose and localize practically every tumor and in the early stages. When all other signs and symptoms fail in the localization, cerebral pneumography will make the diagnosis and localization with precision and without equivocation; and when a tumor is not present, it can be excluded by the same method."

"The operative approach will be dictated by the precise localization. The approach should afford adequate room, and it should be directly over the tumor. After correct localization all brain tumors should be disclosed at operation."

"Every effort should be made to cure the patient by complete extirpation of the growth. There is less mortality from carefully performed tumor extirpations than from unsuccessful explorations for tumors. When, for any reason, it is impossible or unjustifiable to remove the tumor, the maximum palliation should be given at the same operation."

"Decompressions routinely performed are among the most harmful and indefensible operations in surgery. They should never be performed for unlocalizable tumors; they are the exact equivalent of giving morphine for abdominal pain. The symptoms are masked until it is too late. Decompression should be performed only as a last resort when the tumor cannot be removed and then only after the location of the tumor is known; for in half the cases of brain tumor, no good can possibly be derived from a decompression."

"About 50 per cent of brain tumors can be localized by a neurological examination, and about 15 per cent more can be localized with the x-ray without air injection. In the remaining 35 per cent the injection of air can alone make the localization. It is a dangerous procedure and should be used only when necessary."

Today, twenty-five years later, these revolutionary statements form the background of modern neurologic surgery.

*Acoustic Tumors.*—In 1922 Dandy published a preliminary report and in 1925 a complete work, entitled "An Operation for the Total Removal of Cerebello-Pontine (Acoustic) Tumors." Considering that most frequent tumor of the cerebello-pontine angle is the acoustic neuroma, which is a potentially benign lesion usually easy of recognition, nevertheless it had presented surgical problems which were well nigh insuperable. At the International Congress of Medicine in London in 1913, the three great European surgeons, Horsley of London, Eiselsberg of Vienna, and Krause of Berlin, who had in such large measure been responsible for the birth and growth of brain surgery, presented their results on the extirpation of cerebellopontine tumors to that date. Horsley had ten opera-

tive deaths in fifteen cases (67 per cent), Eiselsberg had thirteen deaths in seventeen cases (77 per cent), and Krause had twenty-six deaths in thirty-one cases (84 per cent). Krause admitted that they yielded the poorest results of all the brain tumor operations. All of the accumulated technical advances of a quarter of a century had made no improvement in the results. At any rate the continuance of an operation carrying such an astounding mortality after such an exhaustive trial was impossible. The reaction came with the publication in 1917 of Cushing's important monograph on acoustic tumors, and with it a modified treatment. He accepted the only conclusion which the foregoing results and experience of his own could justify, that is, "I doubt very much, unless some more perfected method is devised, whether one of these tumors can ever with safety be totally enucleated." He no longer attempted to enucleate these tumors totally but was content to offer a method by which the tumor could be removed partially (intracapsular enucleation). Cushing's contribution was the only important advance in the treatment of cerebellopontine tumors up to that time.

In 1925 Dandy presented his operative procedure by which cerebellopontine tumors can be removed completely. After a thorough and carefully guarded intracapsular enucleation, the capsule of the tumor is painstakingly dissected from the brain stem. In 1934 Dandy introduced the unilateral approach greatly simplifying the procedure. About this procedure Horrax said: "The unilateral approach and total removal has become accepted more and more as the best mode of attack. This method was described first by Dandy in 1922 and enlarged upon by him in 1934."

Not only did Dandy's method allow the complete extirpation of the tumor, but also he gave a scientific explanation of why it carried the minimal mortality. He demonstrated that without doubt the danger of cerebellar decompression is proportionate to the degree of hydrocephalus which is present at the time of operation, and that the removal of the occipital bone at once liberates the pressure in the posterior cranial fossa. But this benefit is at once countered, and may be greatly exceeded, by the injurious effects of the backward pressure on the tentorium (hydrocephalus) and its full force is now exerted without opposition upon the delicate brain stem, jamming it backward. He also demonstrated that when the tumor is removed, the obstruction of the aqueduct of Sylvius is released, and the hydrocephalus automatically cured and its ill effects obviated. This obtains only at times with subtotal intracapsular enucleation.

In his publication of 1934, Dandy made the operation much simpler and safer by removing the outer cap of the cerebellum before beginning the extirpation of the tumor.

And at last he demonstrated that the operation which at once removes the cause not only carries the lowest mortality, but at the same time offers the best immediate and only permanent results because these tumors do not recur. The mortality in removing these tumors is now less than 3 per cent.

*Tumors in the Third Ventricle.*—Up to 1921 a most interesting and important group of benign encapsulated tumors lying within the third ventricle had remained outside the fields of diagnosis and treatment, and therefore the patients with this kind of tumor were condemned to die. On Sept. 30, 1921, the

discoverer of the ventriculography was the first to demonstrate that with the mechanical evidence of the ventriculography it was possible to diagnose and localize the tumors of the third ventricle with the greatest accuracy and certainty, a fundamental prerequisite for their surgical attack.

On October 18 of the same year Dandy was the first to perform an operation extirpating completely a tumor of the third ventricle, with an excellent result.

Later from his surgical experience he collected twenty-one cases, publishing in 1933 his book, *Benign Tumors in the Third Ventricle of the Brain: Diagnosis and Treatment*; all of these tumors had been disclosed at operation and removed.

Up to 1933, from the literature forty-seven tumors of similar character had been reported, but all of these were post-mortem findings, none having been correctly diagnosed during life.

In his book, Dandy presented the three methods of operation that he devised: (1) by the pineal route (posterior approach), (2) by the hypophyseal route (anterior approach) with or without resection of the frontal lobe, and (3) along the midline and anterior to the Rolandic area, used for cysts of the cavum septi pellucidi and cavum Vergae.

*Tumors in the Lateral Ventricles.*—The first primary benign tumor in the lateral ventricle to be found at operation and completely removed was reported by Dandy in 1920. The patient is still living.

The localization was made by ventriculography (on Oct. 23, 1918), after three attempts to find the tumor had been unsuccessful. This happened to be the first brain tumor to be localized by this method.

In 1934 Dandy published his book, *Benign, Encapsulated Tumors in the Lateral Ventricle of the Brain: Diagnosis and Treatment*. In this book thirteen benign encapsulated tumors in the lateral ventricles of the brain are reported, all of which had been disclosed at operation and removed. None of the twenty-five additional cases found in literature had been diagnosed during the life of the patient or removed at operation. He demonstrated that the encapsulated tumors in the lateral and third ventricle are most rewarding exceptions to the ill-founded general rule, which long held neurologic surgeons in restraint, that "every tumor below the surface of the brain is a glioma." Dandy stated that the wisdom of such a rule in the days before accurate localizations of intracranial tumors cannot be questioned, but at the present time a far better dictum is "actually to see every brain tumor (there are occasional exceptions) and to know whether it can or cannot be removed." There are now no tumors giving signs or symptoms that cannot be diagnosed accurately, localized precisely, and disclosed at operation. He demonstrated also that none of the tumors in the lateral ventricles of the brain can be localized from the analysis of the signs and symptoms but all can be localized with absolute precision by means of ventriculography.

*Operations for Trigeminal Neuralgia, Ménière's Disease, and Glossopharyngeal Neuralgia.*—

*Trigeminal Neuralgia:* While developing his operation for the removal of acoustic tumors, Dandy saw the possibility of using the same cerebellar route for

the treatment of trigeminal neuralgia. In February, 1925, he presented his operative procedure by which the sensory root of the trigeminal nerve was sectioned alongside the pons and discovered that all the liabilities of the old operative procedure were avoided. In 1932, Dandy pointed out the following advantages, based on 250 cases, of the subcerebellar route:

1. In no instance had there been postoperative keratitis. The reason for the absence of keratitis, which is one of the principal complications of the temporal route, is that only an instant is required to divide the nerve after exposure under the cerebellum. The keratitis was trophic, as a result of operative trauma to the gasserian ganglion, and this sequel was not due to loss of sensation as had been supposed.

2. The motor root of the nerve was never injured because it is at a greater distance from the sensory root than at any other point of its course. This is all important in cases of bilateral tic douloureux.

3. The seventh nerve was not injured, because it was a safe distance from the fifth nerve.

4. In one out of every twenty cases (5 per cent) a tumor was the cause of the neuralgia and would have been missed if the temporal route had been used. When the tic douloureux is caused by a tumor, it is impossible to differentiate by clinical tests.

Analyzing brain tumors, affecting the fifth nerve, Dandy demonstrated that always the tumor is on the sensory root of the fifth nerve—there being many of them, he found that there is never one on the peripheral branch of the nerve that causes this pain; never is there one at the gasserian ganglion when the attacks are typical.

Dandy made the fundamental statement that only a lesion in the upper neuron, that is between the ganglia of the nerve and the brain stem, can give a paroxysmal pain. In view of this fact, unnecessary peripheral treatments are avoided and the frequently assumed causal relationship of trigeminal neuralgia to peripheral infections is eliminated.

Trigeminal neuralgia has for many years been regarded as idiopathic, but in 1940 Dandy, on the basis of over 500 cases, demonstrated that nearly always there is a very definite underlying cause for it. In 5 per cent of the cases, a tumor or aneurysm will be in the cerebellopontine angle, pressing upon the fifth nerve and causing this pain. In nearly all of the remaining cases an artery will be found on either the under surface or the outer surface of the sensory root.

It is the pressure of this artery upon the bare sensory root that causes the tic pain. This explains why the pain appears in the later part of life; it is when the artery hardens from sclerosis.

Furthermore, in later works, Dandy gave the explanation of a fundamental physiologic fact. When the posterior one-half or even three-fourths of the sensory root of the fifth nerve is sectioned, it is possible to preserve practically the entire sensation of the face and at the same time to cure the pain, regardless of the branch or branches involved. This is due to the fact that, with few exceptions, all the pain fibers are collected in the posterior half of the sensory tract.

Sensations to the face are preserved when three-fourths of a nerve is divided, because of the redundancy of fibers carrying the same function.

*Ménière's Disease:* In 1928, Dandy devised an operation for the surgical treatment of Ménière's disease, publishing a preliminary report with nine cases.

By 1945 Dandy had operated upon the auditory nerve 682 times for Ménière disease, with one death due to meningitis.

At first the nerve was totally divided, but in 1933 Dandy demonstrated that the vestibular branch of the nerve can be divided leaving the auditory branch and consequently not impairing the hearing, in fact, Dandy found that division of even three-fourth of the auditory division of the nerve does not affect the hearing, apparently because of redundant fibers carrying similar functions, and this permits a good margin of safety in insuring destruction of all vestibular fibers that may be included with the auditory fibers.

Dandy stated that in about 10 per cent of the patients with Ménière's attacks both nerves are affected and he demonstrated these facts:

1. After both vestibular nerves are sectioned the gait is normal and the Romberg negative.

2. There are two aftereffects: (a) Jumbling of objects when the patient is in motion; when at rest objects are stationary. (b) Uncertainty, when the patient is walking in the dark.

3. These two disturbances are due to the very intimate association between the vestibular and the visual apparatus in human beings.

At the present time most textbooks carry the statement that Ménière's disease is due to a hemorrhage in the internal ear (Ménière's original demonstration in one case) but Dandy demonstrated the following fundamental facts:

1. Since both the vestibular and cochlear divisions of this nerve are involved, it is evident that the lesion is in the nerve itself and cannot therefore occur in the semicircular canals.

2. The causative lesion must be in the nerve and not in the end organs because the attacks are paroxysmal.

3. The attacks of Ménière's disease are unquestionably similar to the paroxysmal attacks in trigeminal neuralgia, glossopharyngeal neuralgia, and epilepsy.

4. A peripheral lesion cannot cause recurring paroxysmal attacks. Always a higher neurone, and never a peripheral nerve or end organ, is the site of the lesion causing paroxysmal attacks.

5. The cases of vestibulitis following mastoid infection are quite dissimilar in that the dizziness is continuous until the infection is over, and then does not recur in paroxysmal attacks.

The pathology of Ménière's disease has been studied rarely and the few reports have been concentrated upon the semicircular canals. In 560 cases exposed at operation, Dandy found (1) tumors at the vestibular nerve in ten cases (2 per cent), (2) an encircling artery constricting the nerve or a large artery lying upon it in 20 per cent, and (3) no gross lesion visible in the remaining cases.

Dandy called it pseudo-Ménière's disease when they are exactly the same dizzy attacks, but without unilateral loss of hearing and without tinnitus. Dandy

stated that it is quite probable that pseudo-Ménière's disease is, at times at least, only a beginning Ménière's disease in which the tinnitus and deafness have not yet appeared.

In 1939, Dandy published an experimental study of the central connections of the vestibular pathways. He found that the results following section of the vestibular nerves in animals are completely different from those obtained in human beings, therefore, their transfer to man is impossible. In this experimental work Dandy demonstrated five points:

1. Section of either eighth nerve results in frequent spells of violent whirling of the body always to the side of the lesion.
2. Section of both nerves results in violent whirling to either side.
3. After removal of half or all of the cerebellum there is no whirling movement.
4. After section of the eighth nerve and removal of the cerebellar lobe of the same side, violent rotation follows and the whirling is to the same side.
5. After section of one eighth nerve and removal of the opposite cerebellar hemisphere no whirling results. The central control of whirling movements, therefore, is contralateral to the eighth nerve.

*Glossopharyngeal Neuralgia.*—Up to 1927, the operations employed in glossopharyngeal neuralgia had been of the peripheral type. Besides the difficulties of isolating the ninth nerve in the neck without injuring the vagus, the objection remained that regeneration of the nerve is certain to follow its division peripherally.

On April 6, 1927, Dandy was the first to perform an intracranial section of the ninth nerve in the posterior cranial fossa for this disease—an operation almost devoid of danger, and productive of permanent cure without disability.

The first accurate knowledge of the function of the glossopharyngeal nerve was obtained by Dandy when he divided the nerve intracranially.

Isolated loss of function of the ninth nerve had not been known. All previous observations had been made on relatively gross injuries either from tumors or trauma. In all of these some fibers of the vagus had been injured as well as the glossopharyngeal nerve, and functions had erroneously been accredited to the latter, which in reality belonged to the former.

Dandy demonstrated that there was no perceptible motor function in the ninth nerve, the pharyngeal muscles being normal after its intracranial section.

Anatomists state that the stylopharyngeus muscle is the only muscle supplied by the ninth nerve but Dandy showed that paralysis of this muscle cannot be demonstrated by any loss of function.

Dandy stated that the ninth nerve supplies taste for the posterior third of the tongue, but does not supply taste to the whole tongue, a view long held by Luciani and by many physiologists even at present.

The sensory distribution of the glossopharyngeal nerve was shown by Dandy to be in the posterior third of the tongue, the anterior lateral and posterior walls of the pharynx, the vallecula, and the pyriform sinus.

*Cure of Pain in Malignant Lesions of the Mouth.*—In July, 1929, Dandy published his work "Operative Relief From Pain in Lesions of the Mouth,

Tongue and Throat." In this Dandy introduced an operation for the complete and permanent relief from pain associated with chronic and malignant lesions of the mouth, nose, tongue, and throat. He stated that there is no other way of permanent relief, when the pain is referable to the sensory domain of both the glossopharyngeal and trigeminal nerves on one side.

Dandy demonstrated that (1) under such conditions the glossopharyngeal nerve and the sensory root of the trigeminus can be divided at the brain stem (Dandy's subcerebellar approach), both nerves being exposed simultaneously in the same operative field; and (2) both nerves can be divided easily, quickly, and with practically no danger to life or function.

*Operation for Torticollis.*—In April, 1928, Dandy devised an operation by which the first, second, and third cervical motor roots were divided intraspinally on each side and both spinal accessory nerves were sectioned in the neck, all at the same operation. He published this work in 1930 under the title "An Operation for the Treatment of Spasmodic Torticollis."

The only modification that Dandy since added to the procedure is to include the fourth cervical motor nerve on both sides. He demonstrated that this definitely adds to the percentage of cures and does not affect the phrenic nerves.

Recently Dandy pointed out the excellent results obtained in a series of fifty operations that he performed.

Dandy stated that in most instances spasmodic torticollis is undoubtedly of organic and not of functional origin.

*Epilepsy.*—Epilepsy had always been considered as an idiopathic disease.

Dandy's experiments on animals, clinical impressions on human patients, observations from a series of operations performed by him on the brain of patients with epilepsy, and post-mortem studies of their brains, have entirely emancipated epilepsy from the diminishing group of so-called idiopathic diseases.

In 1925, through a series of experiments on animals Dandy demonstrated these points:

1. That when the motor cortex of dogs or cats had been injured by an incision or by inclusion of a foreign body, spontaneous convulsions appeared from time to time thereafter.

2. That subsequently after a period of many weeks and months convulsions could be induced by absinth, with from one-third to one-seventh of the dose required to produce convulsions in the normal animal.

3. That injuries to other parts of the brain did not produce results so striking, but suggested a lowering of the convulsive threshold.

4. That the motor cortex once injured thereafter lowers the threshold at which convulsions appear.

5. That in these animals, therefore, just as in human beings, the margin of safety which is the difference between the normal and the epileptic condition is permanently lost when a cerebral lesion of long standing exists.

From a close study of a large series of patients with epilepsy resulting from tumors of the brain, Dandy observed that clonic convulsions, whether Jacksonian or generalized, are due to those tumors which are localized in the cerebral hemispheres, that is, excluding the brain stem and cerebellum.

The series of experiments on dogs, reported by Dandy in 1927, explains the reasons for these conclusions. In these experiments Dandy demonstrated several facts:

1. Clonic convulsions were induced by faradic stimulation of the motor cortex or subcortex but not cerebellar hemispheres.
2. When, during a localized clonic convulsion, the motor cortex of the contralateral side is excised by a sweep of the knife, the convulsion instantly and completely ceases.
3. When, during a generalized clonic convulsion, the motor cortex of one side is excised by a sweep of the knife, the contralateral side instantly ceases to convulse, but the course of the convulsion on the opposite side is unaffected.
4. When, during a generalized convulsion, the motor cortex of both hemispheres is excised by two rapid sweeps of the knife, the convulsion instantly ceases in all parts of the body.
5. When, after excision of the motor cortex of both cerebral hemispheres, the subcortical motor tracts of either side are stimulated with stimuli of any intensity, clonic convulsions either localized or general could not again be induced in any part of the body.
6. After excision of the cerebellum, stimulation of the intact motor cortex produces clonic convulsions precisely as before the cerebellum was removed.

By these experiments, Dandy showed that (a) only stimulation of the motor cortex or its subjacent fibers (with the motor cortex intact) can produce clonic convulsions; (b) this specificity of function similarly obtains in the human motor cortex and is probably a function of the pyramidal cells; (c) clinical evidence indicates that the attacks of epilepsy, of which the convulsions are a part, may or may not begin in the motor cortex but without the motor cortex, the convulsions could not develop.

In 1925 Dandy emphasized the close analogy between epilepsy and trigeminal neuralgia. Furthermore, in later works, Dandy made the following fundamental statements:

1. The attacks of epilepsy are precisely similar to the paroxysmal attacks in trigeminal or glossopharyngeal neuralgia and Ménière's disease.
2. It is impossible to produce recurring spasmodic attacks of convulsions, of dizziness, or of pain, except by a lesion in the upper neurone.
3. Involvement of a higher neurone is essential for the production of any paroxysmal attacks. Epilepsy cannot be produced by any lesion along the peripheral nerves. It can only result from a lesion in the cerebral hemisphere. From his experimental, pathologic, clinical, and surgical studies, Dandy presented a sufficient number of unquestioned facts to place epilepsy unequivocally upon a pathologic instead of an idiopathic basis.

*Pineal Tumors.*—Up to 1921, tumors of the pineal body had rarely been diagnosed, and almost all had been accidental findings at necropsy. The absence of a correct localization of this lesion had precluded any operative interference with this region.



Dandy's operations for trigeminal neuralgia and for cerebellopontine and hypophyseal tumors.

*Orbital Tumors.*—Up to 1920, the methods of approach to the orbit were often totally inadequate for the removal of orbital tumors. In 1921, Dandy devised an operation which permits removal of combined intraorbital and intracranial tumors. Eighty per cent of orbital tumors extend intracranially; they may arise intracranially or intraorbitally, the former more frequently. Moreover, growths that are restricted to the posterior part of the orbital cavity are much better removed by this attack.

The great advantage of Dandy's operation lies in the much fuller and safer exposure of the intraorbital contents. The optic nerve, the eyeball, three of the extraocular muscles, and the ophthalmic veins and arteries can be exposed and avoided during the dissection of the orbital tumor.

Dandy used, in his operation, the operative approach that he devised for hypophyseal tumors. He found that swelling of the brain that so commonly follows ether anesthesia is avoided when avertin is used, and for that reason the size of the bone flap necessary for the exposure of the base of the brain can be greatly reduced and simplified.

Dandy's transcranial approach carries very little risk, and it offers the maximum hope of cure without cosmetic defects.

For tumors confined to the orbit Dandy's operation offers a far better exposure of the tumor than is possible by any other method and with less injury to intraorbital muscles and nerves. Complete dissection of the tumor is much better done by this approach.

In 1941, Dandy published his book *Orbital Tumors: Results Following the Transcranial Operative Attack*. This book sets a milestone in the study of the pathology and surgical treatment of orbital tumors.

From his wide surgical experience, Dandy presented a series of twenty-four patients with intraorbital tumors operated upon by the transcranial route with a very low operative mortality (4.1 per cent). Of the series of twenty-four tumors 20 per cent were confined to the orbit and 80 per cent were combined intraorbital and intracranial growths.

Dandy stated the following facts:

1. From the clinical examination of patients with exophthalmos it is not usually possible to tell whether or not there is an intracranial extension of the orbital tumor.

2. Frequently the orbital tumor is but a small fraction of the large but silent intracranial tumor, which is usually the primary growth.

3. Only the transcranial approach will offer solution of the problem.

4. Once a tumor has been attacked by an external operative approach, the possibility of cure by a subsequent intracranial approach is greatly lessened and may be impossible.

*Defective Intervertebral Disks.*—In 1929 Dandy published his discovery of two ruptured lumbar intervertebral disks under the title of "Loose Cartilage From Intervertebral Disks Simulating Tumor of the Spinal Cord." These are now practically the commonest lesions on which surgery is done. These were

the first intervertebral disks disclosed at operation and recognized as such. At that time he suggested that they were probably responsible for many cases of sciatica.

In his later publications on this subject (1943-1944) he has greatly simplified the diagnosis and introduced improvements that have insured permanent cures. He and his staff have now done operations on over 2,000 disks. He disclosed the importance of the small disks which he called "concealed" disks. Dandy's concealed disks give precisely the same symptoms as the large ones, the only difference being the intensity and persistence of the symptoms, backache with or without sciatica; they comprise three-fourths of the total number. None of these can be detected by contrast media.

Dandy's method to determine which of the disks is involved includes four points:

1. The roentgenogram shows a narrow interspace in 75 per cent of the cases; narrowing of the disk is pathognomonic of a defective disk. (Until recently, defective disks were diagnosed only by injections of iodized oil, air, or other contrast mediums into the spinal cord. Dandy demonstrated that these are never necessary and are always inadvisable, frequently misleading and harmful.)

2. If there is a diminution or absence of an Achilles reflex, the disk will be at the fifth in most instances.

3. The disks at the second and third are usually localized by pain in the front of the thigh; the others give pain in the back of the leg.

4. When these tests are still negative, the affected disks can be localized at operation by horizontal pressure upon the spinous process. This determines the mobility of the joint and a defective disk will usually cause increased movement at the affected joint. The exceptions to this rule are in narrow intervertebral spaces shown roentgenologically; there may then be no mobility or less than normal.

Based on his accurate anatomic, physiologic, and clinical knowledge, Dandy devised his operative procedure proposing the thorough removal of the affected disks after which a fusion of the entire vertebral surfaces results. Dandy stated that the anatomic deviation of the lower lumbar lateral facets is the primary cause of defective disks. He demonstrated the following points:

1. His procedure does what nature attempts to do slowly over many years as is evidenced by the narrowing in the x-ray appearance.

2. After complete removal of disks the fusion of the spinal column is more nearly perfect than the most successful bone graft can be, and at the same time the cause is removed.

3. In the treatment of ruptured disks a spinal fusion by bone graft is never necessary and cannot be too strongly condemned.

In August, 1944, Dandy published his article: "Treatment of Recurring Attacks of Low Backache Without Sciatica." In this fundamental work he makes the following statements:

1. Recurring attacks of low lumbar backache without sciatica have precisely the same underlying cause as backaches plus sciatica, that is, defective intervertebral disks.

2. The diagnosis of defective disks is made solely from the history, the neurologic examination (frequently negative), and x-ray examinations of the spine.

3. Defective disks are multiple at least in 80 per cent of the cases, with or without sciatica.

4. All spinal injections for diagnosis or localization are unnecessary; they are painful and at best make the diagnosis in only 25 per cent of the cases, whereas over 98 per cent can be diagnosed and localized without them. Even simple x-ray films alone diagnose more than 75 per cent. Spinal injections of any type should be strongly condemned.

In January, 1945, Dandy published his work, "The Treatment of Spondylolisthesis." Heretofore the standard treatment for spondylolisthesis has been spinal fusions with autogenous grafts.

Dandy demonstrated these facts:

1. Subjectively and objectively, spondylolisthesis is precisely like defective intervertebral disks, only the x-ray differentiated the two conditions.

2. In at least 90 per cent, and probably all of the cases, there are two or three disks (including the one at the site of the spondylolisthesis) causing the backache and sciatica and a cure depends on the recognition and treatment of all the affected disks.

3. A cure results when the disks are completely removed. The end result of removal of the disks is fusion of the opposing vertebrae and therefore stabilization of the spine.

4. Spinal fusions by grafts are never indicated either for spondylolisthesis or for defective intervertebral disks.

*Rhinorrhea and Otorrhea.*—The first successful treatment of rhinorrhea was reported by Dandy in 1926. Autogenous grafts of fascia lata were sutured over the dural opening behind a depressed fracture of the orbit and the frontal sinus.

Dandy took the fascia from the thigh or from the covering of the temporal muscle. The fascia may be sutured in place or, when this is not practical, laid over the defect.

In August, 1944, Dandy published his work, "Treatment of Rhinorrhea and Otorrhea," presenting eleven cases. Dandy stated that the differential diagnosis can often be made by observing the cerebrospinal outflow:

1. If when the head is tilted forward there is a sudden increase in the volume of fluid, it is apparent that the fluid has been contained in a reservoir and that the fistula is located in a frontal sinus.

2. If the flow of fluid is not altered by tilting the head, an opening in the ethmoid or in the sphenoid cells is indicated.

Dandy's methods by which the fistula may be closed are (1) suturing the dural opening, (2) suturing when possible a transplant of fascia over the dural defect, (3) suturing snugly to the overlying tissues a flap of dura or any soft tissue which has been turned over the bony opening, (4) covering the bony opening with bone wax.

For fistulas through the frontal sinus Dandy devised two methods of approach: one, by elevating the depressed fracture, suturing or covering the defect with fascia, and replacing the depressed fracture; second, if there is no depressed fracture by exposing the frontal region through a unilateral frontal bone flap with a concealed incision, two such procedures are preferable to the single large bilateral exposure, which uncovers and usually requires ligation of the longitudinal sinus.

Dandy states that death following closure of fistula is due to a pre-existing intracranial infection, usually one or more abscesses in the brain.

Eight of the eleven patients whose cases are included in Dandy's report were permanently cured.

Dandy's operation for the treatment of rhinorrhea and otorrhea is practically free of danger.

*Restoration of Nerves.*—In 1943, Dandy devised a method of restoring nerves, requiring wide resections of neuromas in the upper arm. This is accomplished by resection of the necessary amount of the humerus. It could be applicable in other locations though with aftereffects from the shortening.

Dandy stated in this connection, the following beliefs:

1. The same method can be used when a nerve is resected to cure a tumor along one of the nerve trunks in the upper arm or leg.
2. When a tumor is removed with the nerve, the resection of bone should be done at the same time or within a few days thereafter.
3. It is the only way that function can be restored after an interval that permits larger neuromas to form.

*Scaphocephaly.*—In September, 1943, Dandy introduced an operation for scaphocephaly. His operative procedure consisted of enlarging the cranial chamber by lifting most of each side of the skull. He fixed the elevated bone flap by a piece of bone cut from the posterior margin of the flap and wired across the defect.

Dandy stated that it is preferable to operate on the right side first, because the major effect of the cerebral protrusion after the dura is opened is borne by the lesser functioning hemisphere.

*Intracranial Arterial Aneurysms.*—Culminating his brilliant studies of aneurysms, Dandy published in 1944 his book, *Intracranial Arterial Aneurysms*, based on a study of 108 cases with 133 aneurysms. Of this series of cases covering a period of twenty years, sixty-four aneurysms were found at operation and the remaining forty-four were disclosed at necropsy over a period of fifty years.

Up to 1937 no attempt to cure an aneurysm at the circle of Willis by direct attack upon the aneurysm was known in neurosurgical annals. Then Dandy succeeded in the first reported cure of an aneurysm, performing the operation in March, 1937. This was also the first time that an operation had been performed with the diagnosis of an aneurysm beforehand. Since then thirty-six aneurysms diagnosed beforehand (with three exceptions) have been disclosed by Dandy at operation with 70 per cent of cures.

On this basis Dandy concluded that a high degree of accuracy in diagnosing aneurysms can be obtained, and the results are much better than the character of the lesion would have indicated. Dandy demonstrated three requirements:

1. An absolute prerequisite to any form of treatment of an intracranial aneurysm involving the internal carotid or its branches is the knowledge of potential collateral circulation through the anterior cerebral and posterior communicating arteries. This is determined by the Matas test, that is, the obliteration compression of the internal carotid artery in the neck by the finger.

2. If this temporary occlusion cannot be tolerated for ten minutes an attack upon any type of aneurysm would be fatal probably, or at least the patient would be left permanently crippled, for in the vast majority of aneurysms treated surgically the internal carotid must be occluded intracranially.

3. An adequate collateral can be established by partially occluding the internal carotid with a band of fascia lata, reducing the lumen about one-half. Ten days later total occlusion can then be done without risk. In this fundamental book Dandy presents the six methods of operation that he devised: (1) Clipping the neck of the aneurysmal sac; (2) trapping the aneurysm between two intracranial clips; (3) trapping the aneurysm between an intracranial clip and a ligature in the neck; (4) excising the aneurysm and closing the entering vessel; (5) opening the aneurysm and quickly inserting a piece of muscle large enough to fill the sac; the muscle then coagulated with the electrocautery; (6) turning back the aneurysm and coagulating the neck of the sac and the aneurysm itself.

In these operative procedures Dandy used the concealed incision that he devised for the hypophyseal tumors. He believed the following to be true:

1. One of the greatest risks attending any treatment of intracranial carotid aneurysms is injury to the posterior communicating artery.

2. If both the internal carotid and the posterior communicating arteries should be sacrificed, the entire circulation of the brain must be carried from the opposite side through the anterior communicating and anterior cerebral arteries, and this link may or may not be adequate.

3. Simple ligations of the cervical internal carotid may occasionally affect an aneurysm, but is usually ineffective.

4. Without actual exposure of an aneurysm, the diagnosis cannot be established; the carotid ligation may therefore be based in a misconception.

5. Pieces of muscle placed upon or around an aneurysm can scarcely be effective in stopping hemorrhage from a leaking aneurysm, and cannot play any role in curing one. If more direct attack is not possible, the electrocautery is a far better means of closing the point of rupture and offers a chance of cure.

#### SUMMARY AND CONCLUSIONS

I have mentioned only some of Dandy's outstanding works, because it is impossible in an article of this type to comment on all; there are about 200 publications as a result of his thirty-five consecutive years consecrated to neurosurgery.

Dandy wrote the most brilliant chapter in the history of neurosurgery. The extraordinary merit of his works lies not only in making the most important discoveries in his field, but also in the combined experimental, pathologic, and clinical observations from which the end result—their practical application to surgery—is attained.

To gain a clearer and more detailed idea as to how the evolution of neurosurgery was accomplished through Dandy's works, the years since 1910 may be divided into three periods of ten to fifteen years each:

*First Period (1910-1920).*—Among Dandy's varied works there are two epoch-making discoveries: (1) The cause, mechanism, and diagnosis of hydrocephalus done in animals and checked on necropsy and the operations for its treatment; (2) cerebral pneumography; both ventricular and spinal injections.

Dandy's discoveries are the foundation in the modern structure of neurosurgery. Without his discovery of the cause of hydrocephalus, the most important subject in neurosurgery, and his complete experimental, pathologic, and clinical studies, neurosurgery would still be far behind its present development. Since its introduction, many papers have appeared in literature suggesting improvements in techniques and a wider application of the principle, but fundamentally little has been added to Dandy's original conception and description. Although each one of Dandy's works constitutes a transcendent landmark in the history of neurosurgery, obviously his discovery of ventriculography in 1918, making possible for the first time the accurate localization of brain tumors, started a new epoch, not only from the technical point of view, but from the intellectual. It transformed radically and integrally the mental conception of neurosurgery, replacing the existent dogmatism and empiricism with a realistic judgment and authentically scientific criterion.

From the historical point of view, if we realize that the three discoveries of the nineteenth century (antisepsis, anesthesia, and cerebral localization) are responsible for the outgrowth of surgery of the brain and that without them surgery of the brain would never be possible, we also realize that without the most important contribution of the twentieth century (Dandy's discovery of ventriculography), surgery of the brain would scarcely be worth while.

*Second Period (1920-1935).*—In his warfare against neurosurgical ailments Dandy used three different lines of attack, all perfectly synchronized:

1. Since his air injection made possible the diagnosis and precise localization of all brain tumors causing symptoms of intracranial pressure, Dandy revealed the secret abodes of tumors occupying the lateral ventricle and third ventricle and all parts of the brain below the surface. The first tumors of the lateral and third ventricles to be diagnosed beforehand, found at operation and completely removed, were reported by Dandy.

Thus, he radically changed the ill-founded and rather philosophic concept that the normal brain tissue must always be respected and for the first time demonstrated the possibility of removing nonencapsulated brain tumors by extensive resection of contiguous brain tissue, devising the necessary techniques

On this basis Dandy concluded that a high degree of accuracy in diagnosing aneurysms can be obtained, and the results are much better than the character of the lesion would have indicated. Dandy demonstrated three requirements:

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## COMPLETE EXTRACAPSULAR EXCISION OF TUMORS OF THE HYPOPHYSIS

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THE intranasal approach for tumors of the hypophyseal region has been definitely abandoned by all those whose knowledge is up to date with regard to surgery of the hypophysochiasmatic region. Only unjustified stubbornness would favor this approach today, and it should be formally contraindicated in diseases of this region.

The indication for operating on tumors of the hypophyseal region is given by their influence on the optic tract. Patients are not operated upon to correct endocrine disorders, but to prevent amblyopia and blindness, and also, eventually, to prevent or diminish endocranial hypertension. This can result from a blockage of one or both foramina of Munro, due to the upward growth of the tumor, so that by displacement of the third ventricle an internal hydrocephalus is produced. The majority of the cases which are found in practice, and are the cause of joint collaboration between ophthalmologist and neurosurgeon, have various degrees of atrophy of one or both papillae with more or less marked defects of visual fields. As the compression of the chiasmal region is the principal cause for surgical indication, it is obvious that the liberation of that same compression is the chief object of the operation.

The nasal approach, with a field that is septic and of limited space, passes through the sphenoidal sinus to reach the floor of the sella turcica. Even in the best of circumstances, the surgeon will "bite" the inferior pole of the mass, should this be against the floor of the sella, or most probably traumatize the hypophysis while attempting to excise the tumor, because it is usual for the tumor to displace the gland toward the fundus of the hypophyseal fossa. In a few fortunate patients with cysts (craniopharyngiomas) reached and evacuated through the sphenoidal sinus, there has been later, temporary improvement in the visual field, which explains the enthusiasm of some with regard to this approach. However, this access today should be put aside to constitute only a chapter in the history of surgery on the hypophysis.

The extraordinary improvement in neurosurgery has proved that the intradural approach is the best for surgery on the hypophyseal-chiasmatic region. The extensive incisions, which were originally used by Cushing for extradural access to the sella turcica, have given way to small incisions, practically hidden within the limits of the hair, and with which it is nearly always possible to miss the frontal sinus. The visualization of the operative field is obtained with clarity through a series of technical measures not requiring description here, but which have contributed to reduce the mortality to figures oscillating between 5 and 10 per cent, according to the various clinics and neurosurgeons.

Although the method of choice is the intradural route with a small incision, the surgical manner of treating the tumor itself is a fundamental

chapter and we wish to insist on a few ideas which we consider essential. Very often neurosurgeons are content to reach the tumor, incise its capsule, and lightly curette its contents, leaving the rest of the therapy to x-ray treatment. Without doubt, this is not sufficient. The surgeon should go further, recognizing the extraordinary opportunity he has for obtaining more lasting results, perhaps even definite results, by completely eliminating the mass which is pressing on the optic tracts. It is not exactly the intrasellar portion of the tumor which presses against the optic chiasma, but the supra sellar. While the mass keeps within the sella there is no need to operate, and the surgeon should do so only when the tumor has caused visual disturbance. Usually the tumor also grows behind the chiasma and presses against its posterior aspect. If we should leave this portion of the tumor, and content ourselves with the excision of the anterior or intrasellar portion of it, we would be committing a grave error. Our ideal is to excise the tumor with its capsule. This can be done only in a few cases (Case 1). Usually the capsule of the intrasellar portion of the tumor is intimately adherent to the lining of the sella turcica and this makes its extraction impossible. In these cases, the tumor should be curetted, and should there exist a suprasellar or retrochiasmatic portion, it should be excised. Blind curettage of the tumor frequently causes serious trauma to infundibulum, which is in close contact with the mass. It is necessary to apply traction to the capsule so that it may be dislodged from the posterior aspect of the chiasma and drawn toward the anterior part of the sella, normally occupied by the stalk of the hypophysis, and only then should its contents be curetted and all possible eliminated from the capsule. It is hardly necessary to say that while work is being done close to the hypothalamic centers and the arterial circle of Willis, all this should be done very delicately.

In cases of adenomas, the total extracapsular excision is rarely possible, but may be obtained, as was managed in Case 1. In craniopharyngiomas, total excision is also possible. In many cases, the predominant mass is intrasellar and the capsule and dura intimately fused. In others, the mass has grown chiefly upward, adhering intimately to the infundibulum, and any effort at extracapsular extraction is impossible, because it would doubtlessly produce the death of the patient. Radiotherapy alone can produce acceptable results in the treatment of adenomas of the hypophysis, but is useless in other benign tumors.

X-ray treatment would be justified in adenomas, when the diagnosis for this type of tumor is sure and the optic tracts only slightly altered by the compression, and with the condition that visual field control can be checked periodically. Radiotherapy may cause sudden limitation of visual fields: then the operation should be done without losing time. Today we consider that x-ray treatment should be only the complement of the operation. Its formal indication is in those cases in which, for general reasons, an operation is contraindicated and should be done with all possible care. X-rays are not used, of course, when extracapsular excision has been performed. Postoperative

radiotherapy is indicated routinely in adenomas of the hypophysis, whatever their histology. X-ray treatment is also indicated in small doses in the postoperative treatment of craniopharyngiomas, because it seems to have a certain inhibitory effect on the production of cystic fluid.

### CASE REPORTS

**CASE 1 (Clinical History No. 20239).**—The patient, aged 21 years, was a man from Argentina.

**History of Illness.**—Five years before admission he had frontal headaches, usually very slight. At times they were strong. During the month before admission he had headaches four to five times a week. He could see little with his right eye for the last two years, and could not read the papers. He was given eyeglasses, but his sight did not improve. During the last two months it became rapidly worse. Asthenia was present and he had little inclination for work.

**State of Health at Time of Admission.**—His general condition was good, with indifferent decubitus. Nerve I, sense of smell was diminished on the right side.



Fig. 1.



Fig. 2.

**Fig. 1 (Case 1).**—Dandy's incision of approach to the hypophysis; totally hidden within the limits of the hair. An extracapsular excision of a cystic chromophobe adenoma was performed on this patient.

**Fig. 2 (Case 1).**—Cystic adenoma of the hypophysis; completely excised.

Nerve II, right eye, showed atrophy of papilla. Left eye, the superior aspect of the papilla was diffuse and veiled, slightly hyperemic. The retina surrounding the superior pole showed the striation of the nerve fiber layer (edema that elevates the internal limiting membrane of the retina) and slight venous traces, bilateral hemianopsia. Nerves III, IV, and VI, extrinsic ocular movement was normal. Nerve V, facial sensibility was preserved. Cranial reflexes were normal. Nerve VII, facial movement was preserved. Nerve VIII, hearing was good. Nerves IX, X, XI, and XII, nothing unusual.

Active movement was preserved. Passive movement revealed nothing in particular. Sensibility was good; there was no ataxia, dysmetria, nor adiadosokinesis. Reflexes: Patellar, sharp; cutaneous, normal. Psyche was good; standing and walking movements were good.

Clinical diagnosis was tumor of the hypophyseal-chiasmatic region.

**Operation.**—Operation was carried out,\* Dec. 16, 1940, under local anesthesia. Dandy's incision for operation of hypophysis was used, totally hidden within hair limits (Fig. 1). The osteoplastic flap was retracted, and no sign of endocranial hypertension was observed. The chiasmatic region was reached with relative ease. The right optic nerve was found somewhat

\*Assistants, Dr. Veppe and Dr. Calzaretto, instrument nurse, Miss Samper.

flattened and in vertical position. Immediately behind it, part of the surface of the tumor could be seen, of reddish-blue color and smooth surface. With bayonet forceps the capsule was perforated and found to be a cyst. Its contents were aspirated and, slowly, traction was applied to the capsule. For some time, we thought it impossible to extract, and considered the possibility of having to sacrifice an optic nerve, but luckily, while continuing the traction, we were surprised to find that the forceps dragged the tumor out whole. It was a cyst of  $1\frac{1}{2}$  cm. in diameter (Fig. 2). The width of the wall about  $1\frac{1}{2}$  mm. Its anterior surface was smooth and whitish. The hemorrhage which followed extraction of the capsule was only slight and stopped spontaneously. There was never excess pressure applied to the cerebral surface or the infundibulum. Sutured with silk. The bone was fixed with one wire stitch. The patient left the operating room in excellent condition. Pressure maximum 11, minimum 8, pulse 104 per minute.

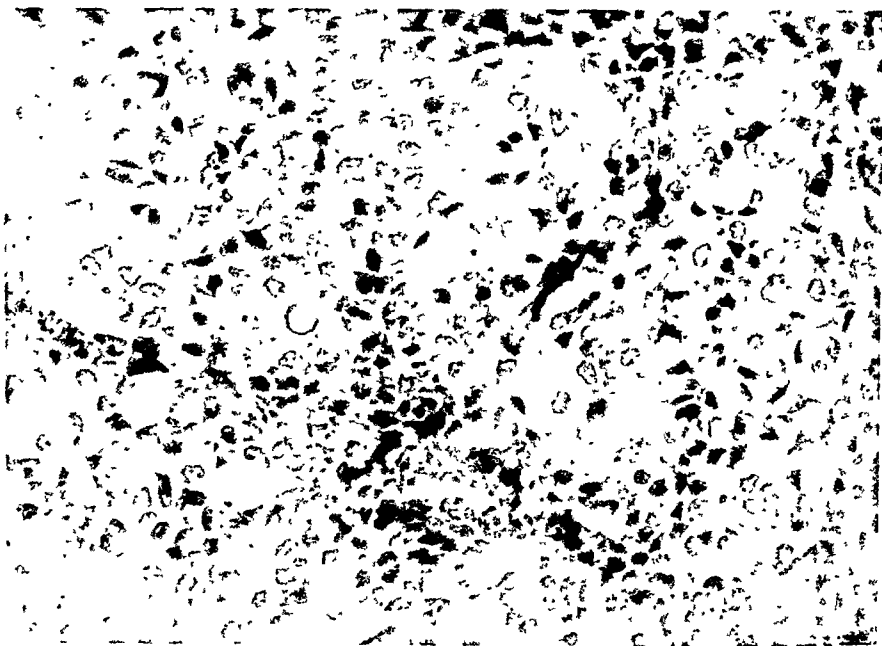


Fig 3 (Case 1).—Cystic chromophobe adenoma of the hypophysis.

*Postoperative.*—The postoperative course was uneventful. The patient was discharged on the tenth day after operation. Jan. 17, 1941, one month after the operation, he was again hospitalized with intense headache, vomiting and photophobia, pain in the nape of the neck, temperature of  $102^{\circ}$  F., and uneasiness. Rigidity of the neck was found. Kernig's sign was positive. For three days he had a sty.

*Treatment.*—Treatment consisted of suppression of liquid and solid intake, subcutaneous hydration, and sulfapyridine, 3 Gm. A lumbar puncture was performed at 7 P.M., and 40 c.c. of purulent liquid were extracted. The spinal canal was washed with saline solution, and 40 c.c. of antistreptococci serum were injected in this way. Sulfonamide treatment was continued. Jan. 21, 1941, the patient was very much improved and afebrile. Feeding was started. The patient was discharged on February 1.

Dec. 30, 1942, the patient was well, with the exception of the diplopia due to the palsy of the right rectus inferior. Paralysis appeared after the acute meningitis, one month after the operation. Surgical correction was done.

Aug. 12, 1945, the general condition of the patient was excellent. In spite of the operation performed on his eye, diplopia did not disappear entirely but vision improved. Although hemianopsia was less, the visual field was still defective.

*Pathologic Report.\**—Cystic chromophobe adenoma of the hypophysis (Fig. 3).

\*By Dr. Pío del Río Ortega.

Case 1 shows the possibility of a complete extracapsular excision of an adenoma of the hypophysis. The late postoperative infection was cured with sulfonamide and antistreptococci serum intraspinally. At that time sulfonamide treatment had just been started in our country. Diplopia was a sequel of meningitis.

Although there was an important improvement in the vision, this case shows that the hemianopsic defect may be permanent if the patient is operated upon late. This was a very rare case of cystic adenoma of the hypophysis.

CASE 2 (Clinical History No. 25052).—A married man, an Argentine aged 42 years, was admitted on April 2, 1943.

*History of Illness.*—About one year before admission the patient began having frontal headaches in the mornings, localized in the supraorbital region, retro-ocular. After 6 P.M. the pains diminished, disappearing completely at about 9 or 10 P.M. when patient lay in bed. He did not vomit. Simultaneously with the headaches, there was decreased libido, that soon became absolute. Before the onset of the present disease, the patient was hypersexual, and practiced daily coitus. For the four months before admission the patient noticed a decrease of sight in the temporal sides of both visual fields, especially the right. He slept more than normal. His weight was constant. There was no alteration in micturition, in frequency or quantity. His appetite was good.

*State of Health at Time of Admission.*—His general condition was good. Cranial Nerves: Nerve I, sense of smell was good. Nerve II, the fundus oculi of the left eye was normal. The right eye showed slight atrophy of the papilla. In the visual field there was bitemporal hemianopsia, of the left eye 1, of the right eye 1/10. Nerves II, IV, and VI, good extrinsic ocular movements. Nerve V, facial sensibility was preserved. Cranial reflexes were present. Nerves VII, VIII, IX, X, XI, and XII were without alteration.

Active movements were preserved. Passive movements were normal. Sensibility was good. Stereognosia was preserved. There was no ataxia, dysmetria, nor adiadokocinesis. Standing and walking movements were normal. Psyche was without any symptoms.

*Probable Diagnosis.*—Tumor of the hypophysis.

*Operation.*—Operation was carried out April 13, 1943.\* A right Dandy's incision was used for the hypophyseal approach. There was an abundance of cerebral spinal fluid in the subarachnoid spaces. It was evacuated, facilitating the operation very much. The chiasmatic region was easily reached, and a round, smooth, reddish-gray tumor, emerging like a helmet, was found between both optic nerves. The tumor extended upward, touching the infundibulum. The right optic nerve, which should be horizontal, was nearly vertical. After electrocoagulation of a few vessels, the capsule was cut and an ochreous-colored fluid flowed out. The tumor was cystic. Bit by bit the traction of the capsule gradually drew it forth in various pieces. The breadth of the capsule was between 1 and 2 mm. Once the tumor was extracted, it was found to be situated on top of the diaphragm of the sella turcica, between this, which had been displaced down, and the hypothalamus. It was thought to be a craniopharyngioma. The operation was well tolerated. The bone flap was fixed with a wire stitch. Sutured with silk.

*Postoperative.*—After the second day, the temperature was high, reaching 104° F., with such excitement, that it was very difficult to keep the patient in bed. He was in a state of fury. For five days he continued the same. At the beginning this state of excitement was not understood, with the possibility of it being a hyperacute infectious process. A lumbar puncture was done, revealing xanthochromic fluid. The bacteriologic examination was negative. After the third day, treatment with sulfathiazole was started, and on the sixth day it was changed to sulfadiazine. Suddenly, this same day, the patient's temperature fell until it reached normal. He was given 18 Gm. of sulfathiazole and 12 Gm. of sulfadiazine.

\*Assistants, Dr. Veppo and Dr. Benchimol.



The impression was that the temperature was not influenced by sulfatherapy and was not of infectious origin. The hyperthermia was believed to be of hypothalamic origin. On the tenth day there was again a sudden rise in temperature, to 102° F., which disappeared on the following day. The wound healed by first intention.

*Pathologic Report.*\*—Gliopithelioma (Fig. 4).

The patient was discharged May 7, 1943. On July 21, 1943, his general condition was good. For the previous fifteen days he had resumed his normal duties. He slept well, but the complete lack of libido continued. Sight was much improved.

December, 1944, at re-examination, visual fields were found normal. Lack of libido continued.

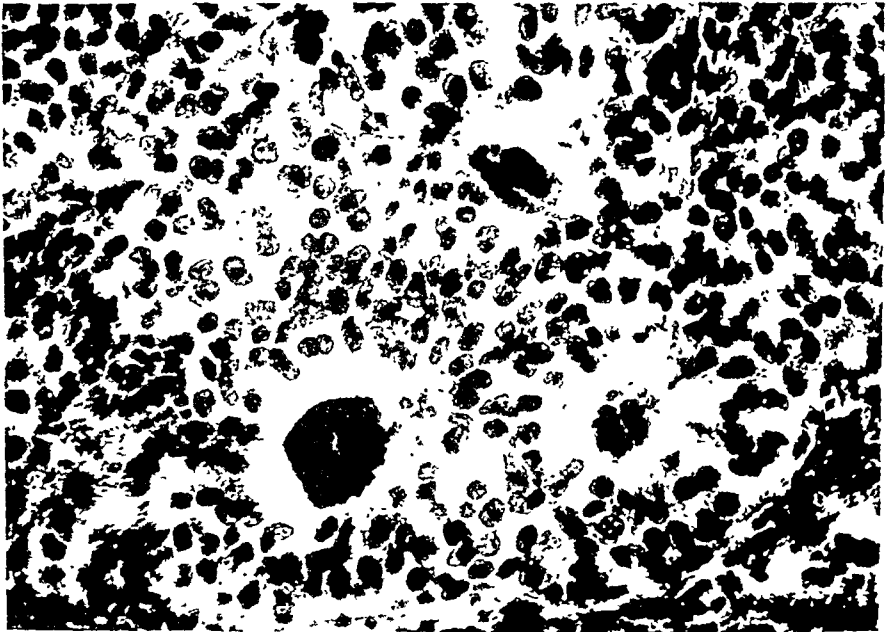


Fig. 4 (Case 2).—Gliopithelioma of the suprasellar region.

This case gives cause for ponderance on some points considered important. Among the symptoms taken in the history was the lack of sexual desire in a man who was previously hypersexual.

Papers by Bard, Dempsey, and Rioch, Brookhart, Day, and Ranson, etc., have made known to us the role played by the hypothalamus in the functional and structural integrity of the genital organs.

Vidal, working with white rats, proved that the destruction of both supra-chiasmatic nuclei produces the lack of sexual desire in males. With regard to females, it was principally found that they lacked acceptance of the males.

In this patient (Case 2), the tumor was situated in contact with the anterior part of the infundibulum at the level of the supra-chiasmatic zone, which explains the loss of libido, and at the same time corroborates the experimental work of Vidal.

It may be recalled, also, that in the postoperative period there was a state of marked agitation so intense, that at times it was a problem to keep the

\*By Dr. M. Polak.

patient in bed. Today, it is accepted without discussion that the lateral hypothalamus exercises a fundamental control in regulating the sympathetic-adrenal system, and plays an important part in emotional conditions, anger, fear, etc.

The right lateral hypothalamus was probably contused in an attempt to excise the tumor, because both adenoma and infundibulum were in close contact. Possibly this is the explanation of the state of fury of our patient, more intense than we had ever seen before.

This picture is wholly different from psychomotor excitement that may follow cerebral operations, and is comparatively common.

#### SUMMARY

Two cases are presented: one, a cystic chromophobe adenoma of the hypophysis, and the other, a glioepithelioma of the suprasellar portion; both were excised with their capsules following the rules given for this operation by Dr. W. E. Dandy.

The loss of sexual desire in one of the patients must be attributed to lesions of the suprachiasmatic centers of the hypothalamus, whose experimental destruction in white rats, produces loss of sexual desire in males and lack of acceptance of the male by the female.

The great excitement in the postoperative period may be due also to a lesion of the lateral hypothalamus.

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## CRANIAL NERVE SURGERY IN THE POSTERIOR FOSSA

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REVIEWING the history of surgery one comes to the conclusion that history of surgery is history of wartimes. The great art of surgery was born on the battlefield and at all times surgery has been trying to keep up with the pace of warfare.

The majority of the great surgical pioneers have known days of war, working in or behind the front lines. Surgeons and soldiers have at all times marched and advanced together, both making quick progress in wartime, both making a tragic and often desperate balance between human destruction and human repair. Saving one young life out of a mass of hopelessly wounded soldiers has always been a human ideal strong enough to arouse the minds of the great surgical pioneers, finding on the battlefield new methods to heal. Tamponade; ligature of the vessels; wound disinfection; treatment of wound gangrene; amputations; splinting of broken bones; transplantation and grafting methods; acute surgery of the cranium, the trachea, the thorax, the abdomen, and the bladder; blood transfusion; and even the development of anesthesia are all counteractions of the surgical pioneers fighting for that tragic balance between human destruction and human repair.

A surgical task which seems absolutely hopeless and useless in peacetime becomes in the next war a routine procedure. As old-time surgery was rooted in the battlefield, so are all the offspring—all date back to times of warfare. Neurosurgery, as the youngest and perhaps most revolutionary descendant, not much older than 40 years, is still old enough to be able to look back on several national wars and on two world wars. Maybe this revolutionary child needed a revolutionary time to grow up and be accepted by the medical profession, breaking with old-fashioned ideas and surgical opinions, and overrunning surgical barriers with the fighting spirit and with the speed of action of a warfaring mind. What seemed impossible was simply done in a new way. Drenched and soiled with the blood of so many young lives, lost in several wars of this so highly explosive and war-bound century, the surgical field became more fertile again and the fertility of the field stimulated anew the minds of the pioneers, bringing on a new surgical era.

This new art of surgery needed indeed new courage and precision, often found in times of war. Surgery of the cranial nerves, particularly in the cerebellopontine angle, is also a real child of this daring century. These children grow up fast and simply do what their parents hardly dared think of. What Jules Verne so passionately dreamed in the nineteenth century, missing the revolutionary technique of the twentieth century, may be compared with the ideas of Charcot, the great member of the French medical academy, who claimed in 1860 that the sectioning of the acoustic nerve in the cerebellopontine angle should stop the attacks of vertigo, described by his great colleague Ménière, as well as with the aspirations of the pathologist Virchow, who traveled all over

Europe in 1900 and visited surgical centers claiming that the intracranial meningiomas could be removed before death came on. The American profession, grounded in the new medical clinics of the twentieth century, accomplished, with great courage and precision, what the old medical world thought hopelessly impossible. Neurosurgery born on the old battlefield of Europe, but not well accepted by the old medical society, needed adoption and education by the daring American profession, working independently with a frontier spirit in newly designed laboratories and in special operating rooms. Once accepted in the country of the great experts, who were courageous enough to risk anything for the benefit of one medical solution, who dared to concentrate themselves on just one small medical sector, this youngest child of surgery has grown up much more quickly and more prosperously than the older ones had predicted.

The medical profession of today is already preparing for the full and widespread development of this new medical art. In another ten years the young neurosurgeons from all over the world will line up in the neurosurgical field to participate in a new competition which will be decisive for the best methods and the best results of this new coming surgical period.

In two brilliant generations the great neurosurgical pioneers have shown the expanse and fertility of the neurosurgical field. Numerous young men in this postwar medical world are now eagerly waiting to take up their new tasks and labors, to divide the field again and give the full energy of their generation, trained and hardened by this second world war, to the never-ending progress of medical science.

Now that I have done neurosurgery independently for more than ten years—now that I have lived and worked for ten years trying to do neurosurgery as I saw it done in the American clinics, particularly in Dr. Walter Dandy's Neurosurgical Department, I think I fully understand the terrific awe that overwhelmed me the first time I saw Dr. Dandy at work in his operating room. Also, I now understand much better the almost painful anxiety that drove me back countless times to his operating room during the three years I visited his clinic in the Johns Hopkins Hospital. More than ever I should now appreciate the moment I could see again this greatest expert of neurosurgical work, who combines in one hand the breath-taking technique of huge bloody brain resections and the fascinating art of bloodless nerve sections in the so vascular region of the cerebellopontine angle.

My admiration for Dr. Dandy continues to increase year by year! Ten years ago I admired Dr. Dandy much more for his work on the gliomas of the brain than I did for those nerve sections in the pontine angle done so easily and quickly. Each time I was due to leave his clinic I tried to postpone my return trip to my home clinic in Holland, not because of nerve sections, but because I knew I should miss tremendously those magnificent surgical moments when Dr. Dandy removed en masse a huge glioma of the brain. I was very sure I could not see enough of these frontal lobe, right temporal lobe, and occipital lobe resections, because these radical procedures showed me exactly how we young surgeons should deal radically with those many malignant

growths in the brain, preferably in the very early stage of their development. This early stage could be reached, as I had seen, by means of Dr. Dandy's ventriculography. I was sure Dr. Dandy showed me the right way to deal with this most difficult surgical problem. It was great to see the master surgeon being confronted with those terrific bleedings and dangerous operative shocks. He was always, with no exception perfectly sure about his surgical technique and knew the value of a fraction of a second. He never gave up, and never missed the tumor, but at the same time he never forgot to estimate, with a perfect feeling, the physical condition of his patients.

And this great and real fighter against these infiltrating gliomas of the brain was never too tired to show me the trail which leads to that medical peak where many satisfactory results in brain surgery are awaiting us.

The good results he had to fight for in late cases, we younger surgeons were to find easily in the future, when the medical profession provided us with early brain tumor cases.

That future has become present time and I am very glad I have followed Dr. Dandy's operative technique as closely as possible. My most radical resections for glioma of the brain have given far better results than have decompression operations, counting an average of twenty radical lobe resections for glioma each year.

In one case (my first) I did successfully a right hemispherectomy. However, this branch of neurosurgery is not the most fascinating one. Dr. Dandy developed also another part of neurosurgery which deals with the nerve sections in the pontine angle. Having practiced this technique for ten years, I now realize to a great extent the quality and quantity of expert work that Dr. Dandy has accomplished in the cerebellopontine angle.

In 1932 to 1933 and 1934 I was with some interruptions, in Dr. Dandy's clinic. I knew his operating room better than my living room on Broadway close to the hospital. Weekly I saw one, two, or even three operations in the pontine angle. It was customary for the daily program to start with a partial section of the sensory root (fifth nerve) at the pons for tic douloureux or the partial section of the eighth nerve (vestibular portion) for Ménière's disease, the second operation being the major one, usually for a brain tumor.

One had to be in the operating room just in time in order to see Dr. Dandy make his unilateral suboccipital approach to the cerebellopontine angle.

The rupture and the profuse bleeding of the mastoid vein was a special point of attraction for the visiting doctors; but many doctors never saw this bleeding because Dr. Dandy placed the bone wax in the mastoid stoma quicker than this big vein could produce hemorrhage. Opening the posterior fossa Dr. Dandy took his time, evading the opening of the mastoid cells, this being a weak point in the aseptic approach to the pontine angle.

The drawing of the curtains in his operating room and the very accurate placing of the headlight by his orderly "Bender" warned the late visiting doctors that the first ten minutes of the operation were over. In the next ten minutes Dr. Dandy did the operation. He opened the dura, then the cisterna

magna and cisterna lateralis to procure sufficient room in the cerebellopontine angle; then he sectioned the nerve (eighth or fifth nerve). In his left hand a small brain spatula (Dr. Dandy's brain spatula) and in his right hand a hooked forceps bayonet-shaped), he slipped one or two wet cotton strips in the pontine angle to protect the cerebellum, asked for the suction and the cautery, and in a few minutes the nerve section was done. In case such a section took a few minutes more, Dr. Dandy used to say "gee whizz, this was a hard one" and we all were sure the work done in these extra minutes would have cost us a good deal more time. Nevertheless, in about six weeks we visiting doctors became so familiar with this operation that we could not understand why there was so much discussion in the American clinics about the problem of the partial section of the sensory root of the fifth nerve. Dr. Dandy's approach was a new, perfect method which could be done safely in twenty to thirty minutes, as we had seen in his own clinic. The discussion on the treatment of Ménière's disease seemed finished to us too! The operative treatment was so simple and could be done so quickly, as we had seen, that this section of the vestibular portion had to be considered in the future as the treatment of choice, even for the pseudo-Ménière cases.

In one case, I remember quite well, it took Dr. Dandy one full hour to complete a difficult tic operation. There seemed to be a number of vessels in his way. Several of these vessels had to be thrombosed with the cautery. However everything progressed smoothly. At the end of the operation Dr. Dandy turned round and said: "If you ever run into a case like this one, Dr. Verbeek, you had better close and take the subtemporal route."

This was the first time I felt somewhat uneasy about the suboccipital route to the fifth nerve.

In Dr. Dandy's clinic I saw no serious postoperative complications either in a case of tic or in a case of Ménière's disease in a combined series of 100 operations. In two patients the wound had to be reopened, the patient having developed high temperature and high cell count; accumulation of fluid was found in the operative field. Drainage restored their condition.

Twice in three years I saw a beginning of a keratitis following total resection of the sensory root. The eyelids of these two patients were sutured and the keratitis disappeared readily. These patients were told to wear a special eye-shield for some time. I did not see a facial weakness nor a motor root paresis, and after the *partial* section of the sensory root of the fifth nerve there was still some preservation of sensation for light touch, deep pressure, temperature, and sharp and dull, particularly in the region of the first and second branches. In some cases the cornea reflex was preserved; in other cases this reflex was very much diminished, depending apparently on anatomic variations in the pontine angle (accessory fibers for the cornea reflex).

After having seen some twenty operations for tic and about half as many for Ménière's disease, I thought I was ready to go home. So far as these operations were concerned, I had studied every detail of them; I had made plenty of drawings and taken notes in the operating room; I knew every little movement

Dr. Dandy made during these procedures; I could not miss finding and sectioning these nerves. I was sure these operations would not get on my nerves.

Following Dr. Dandy's advice I went to Philadelphia in the early spring of 1932 to visit Dr. Charles Frazier's clinic. It was a very interesting and enjoyable time I spent in this clinic as in a short time one felt oneself a member of the staff "family," which meant also a member of the Frazier family, Dr. Frazier being a kind father to all of us. Very soon I understood Dr. Frazier was doing a great deal of work—particularly many tic operations following the subtemporal route.

The first operation I saw done was Tic operation No. 690. Dr. Frazier was an expert and his tic patients did very well after the operation. As a rule the patients were out of bed on the fifth day, and left the hospital on the eighth.

Having seen an expert, as Dr. Frazier was, I hesitated to voice objections against his method, comparing this tic operation with Dr. Dandy's method. In a less experienced hand the results of this operation would certainly be less excellent. The following objections might be presented:

1. There was a total anesthesia in the trigeminal area, sensory fibers of which were sectioned behind the gasserian ganglion. The best and most physiologic operation for tic douloureux is the operation that cuts only the pain fibers. (The patients of Dr. Olof Sjöqvist, who performed a tractotomy, had total analgesia of the three branches but also an absence of cornea reflex and thermhypesthesia.)

2. Some of these patients complained very strongly about numbness.

3. The tic patients with pain in the region of the first branch had to have an alcohol injection or a section of the supraorbital nerve.

4. As a whole this subtemporal operation seemed to me more complicated. In each case one had to control the severe arterial bleeding of the middle meningeal artery and the profuse venous bleedings around the gasserian ganglion close to the foramen ovale.

5. Liberating and dividing the sensory root and saving the motor root impressed me as a method requiring long-standing experience.

6. Dr. Frazier told me that in an average of one out of fifty cases he had to do the operation in two stages because of the profuse bleeding, and Dr. Frazier was an expert.

I left Dr. Frazier's clinic still preferring Dr. Dandy's method, but very happy to know the subtemporal route should there be too many big vessels in my way in the cerebello pontine angle. In the summer and fall of 1932 I visited Dr. Harvey Cushing's clinic, the Mayo Clinic, and Dr. Max Peet's clinic. In all these great neurosurgical centers the subtemporal route was considered safer and was used routinely. On my short visits I did not see an operation for Ménière's disease. The subtemporal operation for tic douloureux was in these clinics in very safe hands.

On a second visit to the clinic of Dr. Frazier I was very much astonished to hear Dr. Frazier tell me, "And now, Doctor, I'm going to show you what a poor neurosurgeon I am." I did not know what to say, but I certainly protested.

Dr. Frazier showed me, in the ward, a woman who had a right-sided keratitis, a right-sided trigeminal anesthesia, a right facial paralysis, a complete right-sided deafness, a dysarthria and a marked right-sided ataxia. "Well doctor, what is your diagnosis?" Dr. Frazier asked. Having visited so many good neurosurgical clinics, I did not hesitate in telling Dr. Frazier I thought this woman had a right acoustic tumor in a very far stage of development. Dr. Frazier answered very dryly that this was his first tie case in which he had followed Dr. Dandy's suboccipital route. This was the second time I felt uneasy, and this time very uneasy, about Dr. Dandy's tie operation. I realized that special neurosurgical operations had to be done by special neurosurgical experts.

Dr. Harvey Cushing told me this when talking about the hypophyseal operations. In the winter of 1932-1933 I was back again in Dr. Dandy's clinic, not only to study his radical brain resections for infiltrating gliomas, but also to make myself much better acquainted and, if possible, quite familiar with this wonderful approach to the fifth and eighth nerves.

In any case, I had to master this approach in order to be able to do the operation for Ménière's disease. In 1933 I did not go back to Holland, but remained in the United States until the end of 1934. In these wonderful years spent in Dr. Dandy's clinic, I saw the most radical operations for brain tumors I could dream of and so many operations for tic douloureux and Ménière's disease that I was convinced again that these operations could be done safely. To be exact, I knew of no safer intracranial operation as long as these nerve sections of the fifth, eighth, and ninth nerves were in Dr. Dandy's hands. In 1941 I received a letter from Dr. Dandy telling me he had just lost his first patient with Ménière's disease. It was No. 358. The patient died from a post-operative meningitis. I do not know of any better results in a series of this magnitude. In Dr. Dandy's clinic I saw three patients with neuralgia of the glossopharyngeal nerve. The ninth nerve was sectioned in the cerebellopontine angle, with very good results. In one case the patient proved to have accessory fibers of the ninth nerve, which had to be sectioned afterward, as the patient had a recurrence of this tic douloureux. In between the ninth and the tenth nerve two accessory fibers were found and sectioned. Following this second operation the patient remained completely free from pain.

Writing about cranial nerve surgery in the pontine angle, I should like to express my hope that some day Dr. Dandy will write a book on the removal of the eighth nerve tumors (the encapsulated tumors of the cerebellopontine angle), as Dr. Cushing did for his pupils in 1918. The operative treatment of these benign, well-encapsulated but dangerously located tumors, I consider as the best test for a man's neurosurgical capacities. I know of no more difficult task a surgeon can face. Dr. Dandy practiced the most radical removal of these tumors. In several other clinics the intracapsular excochleation was advocated. Dr. Dandy himself considered the total removal of these tumors as the fiercest battle in the neurosurgical field. Still he chose this battle every time he had to remove such a tumor. I am convinced that only a master surgeon like Dr. Dandy can afford to be in favor of this radical procedure in late cases. Particularly



in a late case, where the tumor has become strongly adherent to the brain stem, I doubt whether this ultraradical removal of the mesial side of the tumor capsule can be advocated as the method of choice for the average neurosurgeon.

Following the thrombosing or clipping of the vessels, which cross from the brain stem to this mesial side of the tumor capsule, the postoperative edema of the brain stem is a complication seen too frequently. I am afraid the mortality would be prohibitive in a long series of these cases. In an early case, there is no doubt, this radical procedure must be the method of choice. Maybe we are approaching the day when the general medical profession is going to recognize this tumor syndrome of the cerebellopontine angle more frequently. A unilateral diminishing of hearing, with or without tinnitus, accompanied with a weakened homolateral cornea reflex or the patient's complaint that dust is always getting into the same eye (same side), will then make more doctors suspicious of the development of a tumor in the cerebellopontine angle.

The unilateral approach to the cerebellopontine tumors, as advised by Dr. Dandy in September, 1934, is, I think, far superior to the bilateral suboccipital craniectomy as generally used for the removal of these tumors. The latter method is not only a far too formidable procedure, taking too much of the patient's already weakened resources, but a unilateral approach provides all the room there is need for. Moreover, the unilateral approach prevents a great deal of mishap, which may occur (in each case of high intracranial pressure) with the wide opening of the posterior fossa. The very dangerous shifting of the midbrain toward the incisura tentorii and the protrusion of the cerebellum through the widely opened posterior fossa, causing hemorrhages and postoperative edema of the midbrain and cerebellum, make the operation unnecessarily hazardous even before the tumor can be attacked.

This protrusion and swelling of the cerebellum and brain stem are also apt to cause a mental change of the patient, not rarely ending in a postoperative delirium, followed again by more protrusion and edema. Likewise, the edema of the cerebellum and brain stem causes poor respiration and poor swallowing, very frequently leading to a postoperative pneumonia. The coughing and difficult expectoration again cause progressive edema of the protruding cerebellum, rapidly closing this disastrous circle. A clear-cut intracranial tumor syndrome deserves a clear-cut and direct route to the tumor, saving a great deal of operative risk. The tapping of the lateral ventricles, the opening of the cisterna magna in order to release as much fluid as possible, the excision of the protruding cap of the cerebellum are all three essential for this unilateral approach. They safely provide all the room there is in the cerebellopontine angle and make the bilateral suboccipital craniectomy entirely unnecessary.

On one point I did not follow Dr. Dandy's technique. Dr. Dandy is in favor of the use of avertin anesthesia with a small additional dose of ether. This anesthesia is perfect, as long as an expert anesthetist\* is administering the ether. In Holland I terribly missed an expert anesthetist, particularly for

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\*Miss G. Smith worked with Dr. Dandy over thirteen years.

these cerebellar operations. Finally, I had to apply local anesthesia. I must say I became accustomed to it and even like it now. In those cases where I needed an additional general anesthetic I tried, one year ago for the first time, 1 c.c. scophedal, injecting this 1 c.c. solution slowly into the transverse sinus. The patient, as a rule, goes to sleep within ten minutes and keeps quiet during the whole operation (one and one-half to two hours). There is no venous congestion in the cranium and the tumor in the pontine angle can be approached much more easily. How much I wish I could forget all the troubles and mis-haps I met, particularly in approach to the cerebellopontine angle during my first years of neurosurgical work in Holland.

Returning to Holland in the early days of 1935 I was very happy to see again, after three years, the old windmills, the dreamy and quiet canals with their old-fashioned sailing boats, and the old dykes, built decades and even centuries ago, but I was frightened when I saw also the old-fashioned operating room where I had had my first years of surgical training in the University Hospital of Groningen. Formerly I was happy in that operating room, working day and night, hoping later to be able to do any operation, no matter how difficult and dangerous. Just like all the assistants I wanted to become an all-round surgeon and in this large University Hospital, where the surgical department was always overfilled with all kinds of surgical patients, I knew I had found the best place for this surgical training.

Educated for general surgery, I left this so beloved operating room in order to study neurosurgery in America. Returning after three years I did not want any longer to become an all-round surgeon.

In the latter the art of surgery becomes so diffused that it loses the sharp and fine character of expert work.

I had been looking forward to a neurosurgical operating room, which, as I soon learned, was not to be built. I tried very hard to feel at home again in this old general surgical operating room. It was the heart of the clinic and I endeavored to get back my old love of this place. All the general surgical work of the University Hospital of Groningen was done in this room. We worked on two tables, when we were rushed with work. This room was also the old-style lecture room or theater for the students, and last but not least this room was used for dressing the wounds of very ill patients.

This operating room with a huge window could not be darkened. My proposal of having curtains in the operating room was not accepted. I knew I would have difficulty doing an operation on a deep-seated tumor or doing a nerve section in the cerebellopontine angle. Nevertheless, when neurosurgical patients were brought to the clinic, I felt I should at least try to do my work, mainly because these patients had no better place to go in this part of the country.

I was so lucky as to remove a left frontal parasagittal meningioma successfully; I operated upon a patient for a pneumocephalus with good result; further, a medullary tumor and also a cystic glioma in the left cerebellar hemisphere were removed in the first two months. These two patients developed bad wound infections, but at length they improved.

Then came my first tic case—a woman suffering from multiple sclerosis and a severe tic douloureux of all three branches of the right trigeminal nerve. Following Dr. Dandy's method I made a right suboccipital craniectomy, the patient being under avertin ether anesthesia. Exploring the cerebellopontine angle, I could just see the eighth nerve but I could hardly distinguish the sensory root of the fifth nerve because the use of the headlight was of very

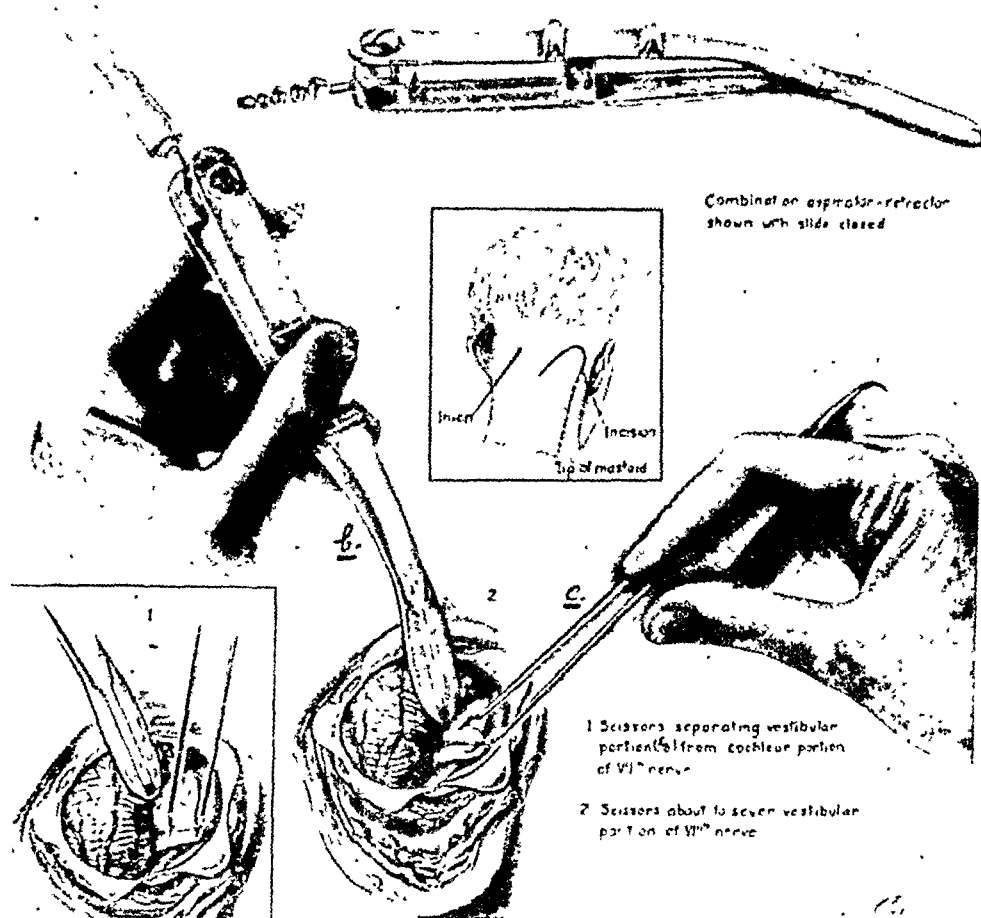


Fig. 1.

Figs. 1 and 2.—Showing the method of using the instruments designed by the author. (These two drawings were made in the School of Artists, connected with the Johns Hopkins Hospital, Baltimore. The original drawing of the operative field was made by Miss Dorcas Hager in 1931; the copied drawing, with the instruments, was made by Mr. Osgood in 1934.)

little help in an operating room that could not be darkened. Moreover, the anesthesia had to be stopped because the patient became very cyanotic. We did not have a special anesthetist for brain operations.

I worked hard for three hours. The patient survived but I had to wait twenty-four hours before she responded again. I am happy to say her recovery was further uneventful and the patient left the hospital within three weeks,

completely free from pain, the wound well healed, and no sign of keratitis nor facial weakness.

I had the same trouble operating on my second tie patient. The anesthesia had to be stopped again, there being much bulging of the cerebellum. Exploring the cerebellopontine angle, I could see the sensory root only very faintly, because the headlight had a very weak focus in this operating room, which still could not be darkened. This operation lasted two hours forty-five minutes. The patient

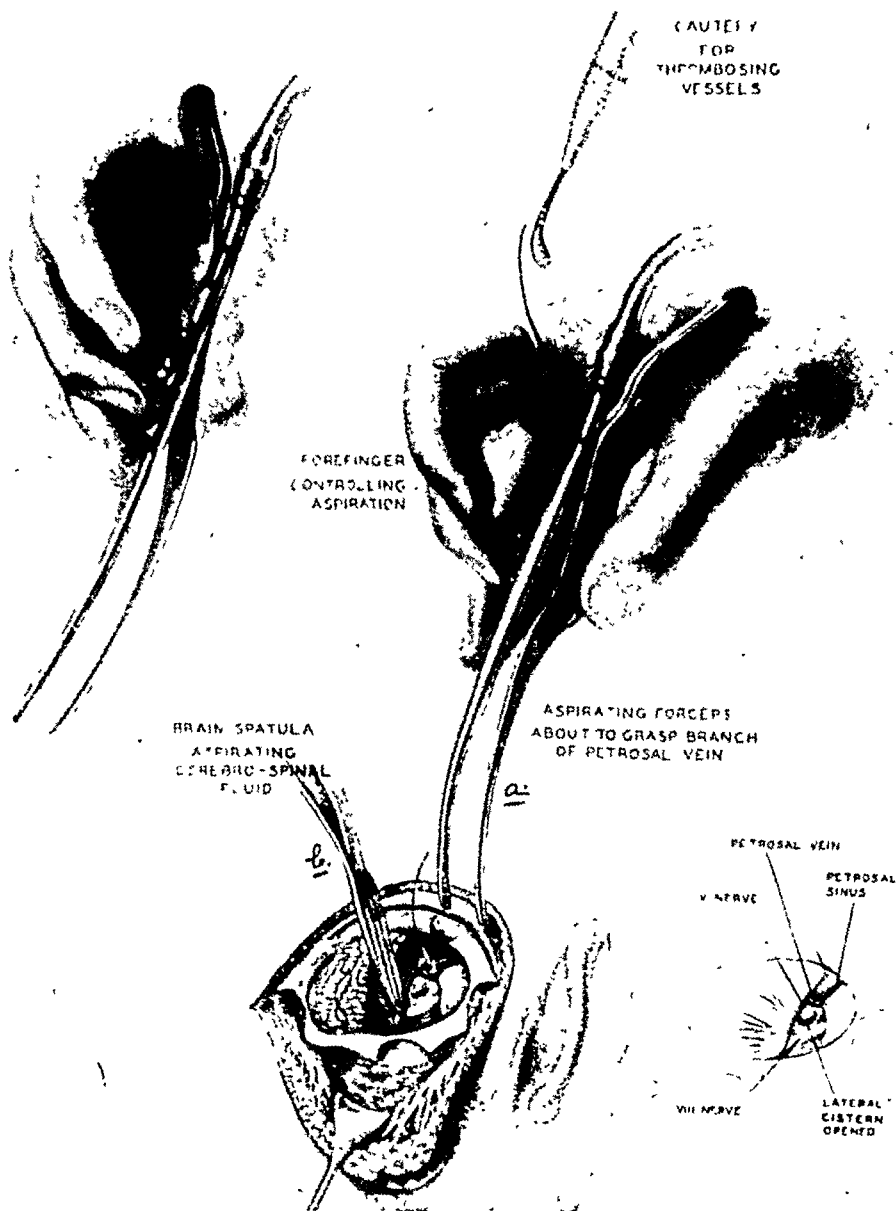


Fig. 2.—(For legend see opposite page.)

did well and was free from pain. Nevertheless, I decided not to operate again on the cerebellopontine angle as long as the operating room was not adapted to this type of work. I endeavored to improve the conditions, did several operations for brain tumors, medullary tumors, meningoceles, and so on, but drifted slowly back to general surgical work. The hospital was to be rebuilt but was not to have a special neurosurgical operating room.

I tried to forget my grievances doing a great deal of general surgical work. If I had not remained in America so long I should certainly have given up neurosurgery. By this time I felt so attached to this specialized work that I could stay away from it no longer.

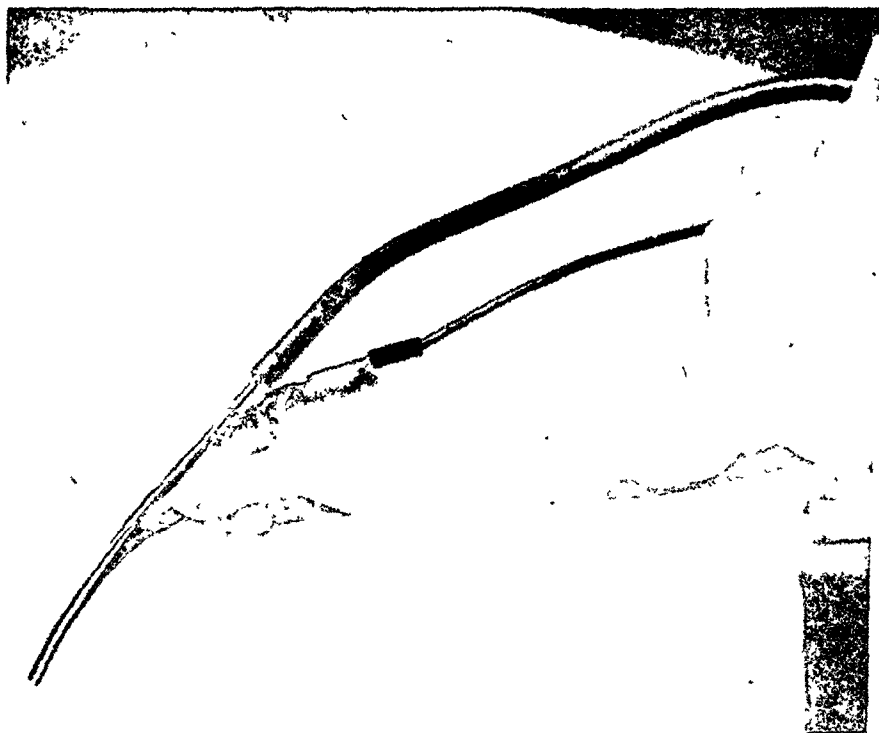


Fig. 3.—The photograph shows the forceps, connected both with the suction apparatus and with the electrocautery.

By the end of 1936 I felt I had done enough general surgery and I decided to start my neurosurgical work independently.

The first thing I asked for when coming to the private Catholic hospital of Gromingen was a special neurosurgical operating room and a special staff of nurses. In a few years the number of patients increased so much, that the Catholic Sisters decided to have also a special neurosurgical department in the hospital with a very modern operating room, which was to be used exclusively for neurosurgical work. In July, 1941, this new department was opened and the work has been increasing very rapidly.

Particularly for the work in the cerebellopontine angle and also for the operations on deep-seated tumors, I have been using two instruments which I designed when I was studying in the Johns Hopkins Hospital.

One instrument is a brain spatula or retractor, which can be used as a suction apparatus. The other instrument is a bayonet-shaped forceps, which is not only connected with the suction, but also with the electrocautery apparatus (see Figs. 1 to 3). Controlling a bleeding in a deep-seated place, I use the brain-retractor with my left hand, exposing the bleeding point and aspirating the blood and the cerebrospinal fluid. At the same time I place the forceps on the bleeding point. This point is then kept dry, because the blood and the fluid are continuously aspirated through a small opening in one leg of the forceps, carrying the suction tube. This forceps is also continuously connected with the electrocautery apparatus. The bleeding point is therefore automatically coagulated, as soon as the forceps is placed on it. The switch for the electrocautery is on the operating table. Having a sudden and severe bleeding from a deep-seated point in a narrow operative field one really does not need much help. The only thing that has to be done is to expose the bleeding point with this brain retractor and place this forceps on the bleeding point; the rest is done automatically. In ten years I have never used a silver clip to control bleeding. Particularly in the cerebellopontine angle, I feel much safer when using these two instruments.

I am perfectly sure Dr. Dandy will smile faintly at the idea of these instruments. He is never worried about any bleeding and, moreover, he knows very well how to avoid bad bleedings, particularly in the cerebellopontine angle. When a beginner wants to examine the sensory root of the fifth nerve, all the vessels in this angle seem to be in the way and several of them are apt to get torn before the sensory root can be seen.

The cerebellopontine angle is really not a location for a beginner. It is a gorge full of pitfalls.

I have done over eighty operations on the cerebellopontine angle. Still I never forget to use my two semiautomatic instruments. I have now done a series of forty operations for trigeminal neuralgia, following Dr. Dandy's method. In another series of ninety-cases I used Dr. Frazier's approach. Now that I have tried both methods I am sure I prefer Dr. Dandy's. It is a more physiologic operation. One is able to cut the pain fibers of all three divisions, preserving a good deal of sensation in the first and second divisions. The absence of the cornea reflex is even less frequent than after the tractotomy (Sjöqvist operation).

To be sure one has to be very familiar with all the technical details of this operation. I had to wait a long time before I could do this operation safely.

#### DISCUSSION

1. The anesthesia is, I think, the main technical point of this operation. If the anesthesia is not perfect, there will be too much bulging of the cerebellum. In such a case it is hardly justifiable to undertake a partial section of the sensory root of the fifth nerve at the pons. I now use local anesthesia (pantocain 1 0/00) with 1 c.c. scophedal, injected into the transverse sinus during the operation.

2. The cerebrospinal fluid must be drained very slowly from the cisterna magna and lateralis cisterna in order to prevent vomiting.

3. The petrosal vein must be thrombosed and divided before the sensory root is exposed. This can be done easily and safely with the help of my instruments.

4. The arterial loops covering the sensory root should, if possible, be carefully held aside. Cauterization is rather dangerous because these loops are too close to the brain stem.

5. This partial section can be done safely only in a dark operating room, the operator using a very good headlight.

6. The dura defect must be closed, either by suturing back the small dura flap or by using a fascia muscle transplant as Dr. Dandy has advised.

In some cases I still prefer Dr. Frazier's operation, particularly for patients with a very short and fat neck, and also for patients who are very old (75 years of age and over) I think Dr. Frazier's method is a safer procedure.

In the Dandy series I lost one patient (79 years old) who developed a postoperative pneumonia. The operation was done under ether anesthesia. Another patient, 62 years old, who had a heart failure, died suddenly on the second postoperative day, complaining much about precordial pain.

In the Frazier series I lost also two patients. A woman of 66 years died in postoperative shock; a woman of 71 years developed a bronchopneumonia. This woman was also suffering from multiple sclerosis.

The intracranial operation I like best of all is the partial section of the eighth nerve for *ménière's* disease. I have now performed twenty-seven of these operations. All the patients are doing well. This partial section of the eighth nerve can be done much more easily than the section of the fifth. The petrosal vein should be left untouched and one hardly needs to retract the cerebellum. As a rule I use only local anesthesia without scophedal. Before sectioning the vestibular portion I warn the patient that an attack of dizziness may be coming, which does not always happen. An occasional vomiting does not disturb this operation. Under local anesthesia there is hardly any bulging of the cerebellum, even when the patient starts vomiting. When the patient is subtotally deaf on one side, I divide the eighth nerve completely, hoping to cure the patient also from the annoying tinnitus. I wish I could start the daily program every day with an operation for *Ménière's* disease. In the last twelve days I did four operations for tic and three for *Ménière's* disease. I operated on two glossopharyngeal tic patients with very good results. Patients with a benign encapsulated tumor in the cerebellopontine angle are not rare in this country. Unfortunately, the majority of them come to the neurosurgeon in the very last stage of tumor development. Therefore I have not practiced the most radical and total removal of these tumors yet. I operated on twenty-one patients. I made a unilateral suboccipital approach, resected a small overlying cerebellar cap, incised the tumor capsule, and curetted as much intracapsular tumor tissue as possible. Then I removed as much of the tumor capsule as possible, leaving the mesial side attached to the brain stem. Except for one, these patients did fairly well after the operation. One patient died three weeks after

the operation from a bronchopneumonia caused by difficulty in swallowing. In two patients the signs of intracranial pressure disappeared only partially. I operated a second time and extended the suboccipital craniectomy bilaterally with good results. In the next twenty years I hope to operate very radically on these benign tumors in an early stage of their development.

#### SUMMARY

1. The development of intracranial surgery, particularly in the cerebello-pontine angle, is briefly reviewed.
2. The operations for lesions of the cranial nerves in the cerebellopontine angle are discussed.
3. A series of 130 operations for major trigeminal neuralgia is reviewed.
4. In a series of forty cases Dr. Dandy's suboccipital route and in a series of ninety cases Dr. Frazier's subtemporal route was followed.
5. As a result of these 130 operations I prefer Dr. Dandy's operation.
6. The technical points of this operation are stressed.
7. Two new instruments for intracranial surgery are introduced.
8. The section of the eighth nerve for Ménière's disease, following Dr. Dandy's method, is reviewed in twenty-eight cases.
9. The operative treatment of the benign encapsulated tumors in the cerebellopontine angle (acoustic tumors) is discussed and twenty-one cases reported.
10. The section of the ninth nerve for glossopharyngeal tic done by myself in two cases is described.

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# THE REPAIR OF CRANIAL DEFECTS BY BONE GRAFTING

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## INTRODUCTION

AS LARGE numbers of persons received wounds of the head during World War II, often with extensive loss of bone and damage to the brain, the time is now opportune to review the position regarding the repair of cranial defects and take stock of past results. The loss of portion of the cranial vault from trauma or other cause has always been regarded as likely to have serious consequences. Even if hernia cerebri does not occur, there may be some bulging of the scalp and meninges from an underlying collection of fluid, and pulsations, synchronous with the heartbeat, are usually visible and palpable. Becoming more marked with effort and with lowering of the head, both these conditions become rather terrifying to the patient, and objects of interest to relatives and friends. Provided the dura mater has not been damaged, there is however, no great likelihood of dangerous sequelae, and restoration of the skull is necessary only for cosmetic reasons or for protection of the brain against further injury. When the dura mater has been injured, or portion of it destroyed, then the loss of bone is more serious and may allow adhesions to occur between the brain, damaged meninges, and scalp, causing severe symptoms and real disability. Should the brain have been damaged also, the resultant gliosis and brain scar become adherent to the scalp and a traction diverticulum forms from the lateral ventricle of the same side. Epileptiform fits of jacksonian type are then likely to occur, as well as loss of function, corresponding to the site of the trauma. .

Even if the brain itself has not been injured, changes in character and behavior, headaches, fits, etc., seem to be expected of any person who has "piece of bone missing from his head," and all sorts of dire consequences are supposed to follow a blow on the unprotected area of brain. The patient lives in dread of these consequences and rapidly develops an inferiority complex. Various forms of protective metal and leather pads are often worn under the headgear. An excuse is present for misconduct, and even criminal tendencies and also for shortcomings and chronic invalidism as far as his earning capacity is concerned. Thus, in the absence of specific contraindications, repair of the cranial vault and damaged meninges should be carried out, not only for the relief of symptoms and signs caused by adhesions and brain scars, but also for psychologic and cosmetic reasons, and to obviate the wearing of external protections, such as jockey's caps with metal inlays, etc.

## MATERIALS

The question of the most suitable material for repair of these defects has always been a vexatious one. An excellent review of the subject and the various

substances in use was given by Grant and Noreross<sup>1</sup> (1939). In the earliest case on record, in 1670, bone from a dog was successfully used. Over 200 years passed before any further reports of plastic operations on the skull appeared. Then followed a thirty-year period during which various types of bone grafting procedures, including the use of the outer table of the skull, were advocated. In an endeavor to avoid two operations upon the one patient, plates made from various inorganic substances were then tested with varying degrees of success. Celluloid came first and continues to be employed by many surgeons. Then followed aluminum, gold, and silver. Results with inorganic materials were, on the whole, unsatisfactory to the surgeon and patient chiefly because of sepsis; and to the lay public they never rendered the patient immune from aftereffects. Indeed, the possessor of a "plate in the head" was always regarded with morbid curiosity, and was expected to become epileptic or insane. In Case 18 of this series, where celluloid had been inserted some ten years previously, a cyst had formed between layers and was the cause of severe symptoms.

Autogenous osteoperiosteal or cartilage grafts became popular again during World War I. They were usually obtained from neighboring outer table of the skull and transferred to fill in the missing area by various ingenious maneuvers. In other cases, free grafts were fashioned from tibia, split ribs, sternum, and scapula. However, these bones were not satisfactory donor sites because it was necessary to use several pieces to fill in large defects; a compromise was effected by the use of soupbone or boiled cadaver skull bone which could be cut to any size or shape. Indeed Nafziger<sup>2</sup> (1936) advocated that bone flaps affected by osteomyelitis and intrinsic tumors should be boiled and then replaced to obviate unsightly deformities and dangerous defects.

In 1931, Pickerill,<sup>3</sup> advocated the use of the inner table of the ilium bone; in 1932, I<sup>4</sup> reported two patients treated by this method. The pendulum has now swung again toward inorganic materials. Robertson<sup>5</sup> (1944), using plates from a new metallic element, tantalum, claims to have found the theoretically ideal plastic material which is chemically and electrically inert in the tissues.

In 1944, Kazanjian and Holmes<sup>6</sup> reported thirty-eight patients in whom reconstruction of the frontal bone had been carried out after radical operation for osteomyelitis. When large grafts were needed, these authors had used vitallium strips and plates, tantalum plates, and, in one instance, an acrylic mold. They admitted that inorganic substances were unsatisfactory, because even the newer materials which were allegedly inert caused foreign body reactions in the tissues and had the psychologic disadvantages mentioned previously. They regarded living bone as the ideal material, but because they favored the tibia or the crest and anterior portion of the ilium as donor sites for strips of bone, they only advocated bone grafting for areas less than two and one-half inches in diameter. They were apparently not aware of the method of obtaining large grafts from the inner table of the ilium, which is regarded as the ideal graft for the skull for the following reasons:

1. A large enough portion can be obtained in a single graft to fill in almost any deficiency.

2. It is curved in the correct planes and can be molded further if necessary.
3. Its inner surface is smooth and not likely to become adherent to the underlying dura, even where it has been repaired or replaced by a graft of fascia.
4. Its outer surface of cancellous bone invites a fresh blood supply from the overlying scalp, to keep the graft alive.

#### OPERATIVE TECHNIQUE

The pathologic lesion in the head must be dealt with first. The scalp, whether it be intact or composed largely of scar tissue, must be reflected well beyond the limits of the missing bone, and the dura or its remains must be identified. Where the dura and brain have been damaged, scar tissue and cerebral gliosis should be excised as far as practicable until healthy cerebrum or the ependyma of the ventricle is encountered. The dura must be freed beyond the edge of the defect in the bone and then reconstituted with the aid of a graft of fascia or other substitute, if necessary. A bed for the graft is prepared by removing any irregular or indriven pieces of bone and beveling the edges of the gap; a pattern is made the exact size of the gap from a piece of zinc foil.

For the cutting of the graft an incision is made just above the crest of the ilium, as described by Pickerill<sup>3</sup> (1931). The abdominal muscles and fascia are detached with a knife close to the bone. The periosteum is divided along the inner aspect of the crest, and the iliacus muscle is stripped from the inner table of the bone. It is then retracted medially with a wide-bladed Royle retractor, until sufficient area is exposed to accommodate the malleable metal pattern. This is placed in position with its longest border along the iliac crest and a graft of corresponding size and shape is marked out with a sharp instrument. It is most important to cut through the inner table along these lines with a narrow osteotome first, before separating up the graft, otherwise the field becomes obscured with blood and the limits of the graft cannot be seen. A wide chisel, with a slight degree of flexibility or curvature, has been found most suitable for cutting through the diploe evenly. Bleeding from the ilium bone is controlled with Horsley's wax, and the wound is then closed with a soft drain which is left in for thirty-six hours. The graft itself can be trimmed to fit into its bed accurately with strong scissors. In the earlier cases of the series, it was simply fixed in place with absorbable catgut sutures, but since the availability of stainless steel wire, it has been wired into place. The scalp is replaced and the wound closed accurately. Drainage for thirty-six to forty-eight hours is advisable and a large protective dressing should be applied.

#### INDICATIONS

Some of the indications for cranioplasty have already been discussed and along with the remainder, they may now be summarized as follows:

- (1) Post-traumatic fits associated with missing bone, adhesions, a cerebral scar, and traction diverticulum of a ventricle
- (2) Headaches, and the syndrome of the "defective cranial vault," namely, dizziness, lack of concentration, loss of energy, mental instability, and intolerance of noise, etc.

TABLE I. SYNOPSIS OF CASES

CASE NO.	SEX	AGE AT OPERATION (YR.)	DURATION, CAUSE, NATURE AND SITE OF INJURY, AND TREATMENT ELSEWHERE	DURATION, SYMPTOMS, AND SIGNS	ENCEPHALOGRAPHY	DATE AND NATURE OF OPERATION, AND TYPE AND SIZE OF GRAFT	IMMEDIATE RESULT	FOLLOW-UP RESULT	CATEGORY
1	M	8	1 yr.; knocked down by motorcycle; compound comminuted depressed fracture with laceration of brain; right parietal; immediate craniectomy	1 yr.; slight hernia; cerebri; no symptoms; wore Joeky's metal skull cap	Not done	September, 1931: repaired dura not disturbed; ilium graft 4 cm. in diameter	Primary healing	Slight headaches when studying at age 15; killed in action in Army, New Guinea, 1942	Satisfactory
2	M	37	35 yr.; cause unknown; compound depressed fracture and laceration of brain; right parietal; immediate craniectomy	16 yr.; nocturnal fits following blow at site of missing bone; 7 yr.; second craniectomy without relief	Cortical atrophy with meningeal adhesions and cyst formation; no distention of ventricles	November, 1931: excision of subarachnoid cyst, cerebral scar, and adherent meninges; dura repaired with Cargile membrane (Fig. 1) May, 1932; large graft of ilium 8 by 3 cm.; full thickness in center	Primary healing; some relief by third operation; fracture of ilium one month after fourth operation during fit	Occasional headaches; no fits for 8 yr.; no sedatives; continuous work as cleaner; some absorption of graft, January, 1945 (Fig. 2)	Satisfactory
3	M	14	2 yr.; kick from horse; compound comminuted depressed fracture and laceration of brain; left frontal; immediate craniectomy	2 yr.; hernia cerebri; no symptoms; cosmetic defect	Not done	April, 1934; meningeal cyst evacuated; ilium graft 6 by 3½ cm.	Primary healing	Occasional headache; has been 4 yr. in Army (united States Army, January, 1945)	Satisfactory
4	M	20	2½ yr.; motor car accident; depressed fracture with middle meningeal hemorrhage; left temporal; immediate craniectomy	2 yr.; jacksonian fits; once a month average	No definite abnormality of ventricles or cortex	December, 1934: dura mater adherent to cortex; ilium graft 5 by 3½ cm.	Primary healing of skull wound; infection of ilium wound from wax; sinus for 1 yr.	Approximately 2 fits every year, but at continuous work on docks and in railway workshops	Relieved

5	M	23	8 mo.; blow with hammer falling 120 feet; compound comminuted depressed fractures involving eye and orbit, and laceration of brain; left frontal and left orbit; immediate repair	16 mo.; headaches; one fit; serious cosmetic defects; left eyeball in antrum; orbital margin and roof inside cranium; unable to wear glass eye (Figs. 3 & 4)	Not done; plain roentgenograms show extensive damage (Figs. 5 & 6)	August, 1935; removal of some bone fragments; severe meningeal hemorrhage; ilium graft 10 by 5 cm.	Subarachnoid hemorrhage; primary healing; glass eye fitted	Two fits in next three years; no headaches, well since; good appearance; working hard as a timber cutter, January, 1945	Satisfactory
6	M	6	1 yr.; knocked down by motor car; compound depressed fracture and laceration of brain; left parietal; immediate repair	No symptoms; cosmetic defect	Not done	July, 1937; ilium graft 3.5 by 3.5 cm.	Primary healing; infection of ilium wound from wax	Good cosmetic result; not traced since November, 1937	Untraced (satisfactory)
7	M	27	15 yr.; cerebral abscess after influenza; right frontal; craniectomy and drainage	13½ yr.; hernia cerebri; fits, once a month average	Large diverticulum of anterior horn of right lateral ventricle	July, 1937; separation of scalp adherent to brain scar; ilium graft 5 cm. in diameter; March, 1939; excision of brain scar; diverticulum decapitated; graft reinserted	Primary healing; then recurrence of fits; bony union found between graft and skull at second operation	Fits less in frequency; developed diabetes, sustained compression fracture of thoracic spine; died of diabetes, July, 1942	Relieved
8	M	29	7 yr.; motor car accident; compound depressed fracture; right parietal; immediate craniectomy	6 yr.; jacksonian fits every two weeks (average); hemiplegia, worse since second operation elsewhere 8 mo. before	Large diverticulum from temporal horn of right lateral ventricle	August, 1937; foreign body (gauze swab) removed and adhesions freed; March, 1940; cadaver bone graft; 5 by 3 cm. (Fig. 7)	Primary healing; no relief after third operation	No sedatives; no fits since 1940; left hemiplegia much improved, but crippled with rheumatism; roentgenogram shows graft almost intact (Fig. 8) January, 1945	Satisfactory

TABLE I.—CONT'D

CASE NO.	SEX	AGE AT OPERATION (YR.)	DURATION, CAUSE, NATURE AND SITE OF INJURY, AND TREATMENT ELSEWHERE	DURATION, SYMPTOMS, AND SIGNS	ENCEPHALOGRAPHY	DATE AND NATURE OF OPERATION, AND TYPE AND SIZE OF GRAFT	IMMEDIATE RESULT	FOLLOW-UP RESULT	CATEGORY
9	M	7	6 mo.; knocked down by motor car; compound comminuted depressed fracture and laceration of brain; right frontal; after immediate operation, hernia and abscess	3 mo.; meningoencephalocoele, and cosmetic defect; slight headaches	Large irregular dilatation of ventriculum from right lateral ventricle	April, 1938; excision of brain scar and chronic encapsulated abscess; outer table of large fragment used as graft (Fig. 9)	Primary healing	No symptoms; good cosmetic appearance; no absorption of graft (Fig. 10), January, 1945	Satisfactory
10	M	25	11 yr.; fall from horse; compound comminuted depressed fracture and laceration of brain; right frontal; immediate repair	1½ yr.; headaches, severe fits in bouts after exertion; cosmetic defect	Large regular dilatation of ventriculum from right lateral ventricle, still present in December, 1944 (Fig. 11)	November, 1938; excision of depressed fragments, dirt, and brain scar, dural ventriculum decapitated; cadaver graft 9 by 6 cm. (Fig. 12); December, 1944; removal of remains of graft (Fig. 13); ilium graft 9 by 6 cm. (Fig. 14)	Transient arorele; primary healing	No fits, no headaches; enlisted A. I. F. in 1939; fits recurred in the Middle East, 1941, and increased to December, 1944; too soon after ilium graft for prognosis	Unsatisfactory
11	M	13	9 mo.; hit with golf ball when caddy-ing; comminuted depressed fracture; dura penetrated; right temporal; immediate craniectomy	No symptoms; slight hernia cerebri	Early dilatation of right lateral ventricle; no dilatation of ventriculum	January, 1939; dura not opened; ilium graft, 5 cm. in diameter	Primary healing of skull wound; ilium wound infected due to wax	No symptoms; working hard on sheep station, January, 1945	Satisfactory

12	M	26	7 yr.; motor ear accident; compound comminuted depressed fracture; right hemiplegia; right frontal and temporal; immediate craniectomy	5½ yr.; headaches; Jacksonian fits once a month average	Generalized dilatation of right ventricle; no diverticulum	April, 1939; adhesions separated; cadaver graft 9 by 6 cm.	Primary healing	No fits for one year; recurrence on ceasing sedation, in bouts every six mo., in service 3 yr., continuous work as dental mechanic; in February, 1945, graft completely absorbed (Fig. 15)	Unsatisfactory
13	M	18	9 yr.; blow from sheet of iron; compound comminuted depressed fracture and laceration of brain; left parietal; immediate craniectomy	2 yr.; fits, once a week average	Large diverticulum from body of left lateral ventricle	June, 1939; excision of cyst and brain scar; diverticulum decapped; ilium graft 9 by 5 cm.	Reactionary hemorrhage of both wounds; infection of ilium wound (no wax used)	'Reasonably free of fits; may go for six months without one'; working on farm, January, 1945	Relieved
14	M	23	1 yr.; motorcycle accident; compound comminuted fracture with laceration of brain; right frontal; immediate craniectomy	3 mo.; headaches; one fit	No diverticulum and normal cortical pathways	December, 1939; scarred, dura not disturbed; cadaver graft 6 by 4 cm.	Primary healing	Had one fit five months after operation, nil since, worked very hard, no sedatives, roentgenogram shows some absorption of graft (Fig. 16) but clinically firm skull, February, 1945	Satisfactory
15	M	18	8 yr.; fall off horse; compound comminuted fracture with indriven fragment of bone; right occipital; wound repaired only	6 mo.; frequent fits, fields of vision defective; no relief by operation for removal of depressed fragments of bone	Localized cortical atrophy with diverticulum from posterior horn of right lateral ventricle	January, 1940; excision of brain scar and wide decapping of ventricle; cadaver graft 6 by 3.5 cm.	Reactionary hemorrhage; infection, epidymitis, and meningitis; removal of graft; sulfonamides; death	Nil	Unsatisfactory (death)



TABLE I.—CONT'D

CASE NO.	SEX	AGE AT OPERATION (YR.)	DURATION, CAUSE, NATURE OF INJURY, AND TREATMENT ELSEWHERE	DURATION, SYMPTOMS, AND SIGNS	ENCEPHALOGRAPHY	DATE AND NATURE OF OPERATION, AND TYPE AND SIZE OF GRAFT	IMMEDIATE RESULT	FOLLOW-UP RESULT	CATEGORY
16	M	13	1 yr.; diving into shallow water; depressed fracture; right parietal; immediate craniectomy	No symptoms except neurosis	No abnormality seen	February, 1940; dura intact; ilium graft 7.5 by 5 cm.	Primary healing	No symptoms; enlisted in Army, 1944	Satisfactory
17	M	24	6 yr.; hit on head with piece of wood in brawl; committed depressed fracture; left parietal; immediate operation and postoperative hemorrhage	2½ yr.; headaches; right hemiplegia; generalized fits progressing to status epilepticus; bad cosmetic defect with deep gutter in scalp	Large diverticulum from left lateral ventricle; scarred cortex 1 cm. in depth	May, 1940, partial excision of scar; decapping diverticulum; repair of dura; ilium graft 6 by 4 cm.; plastic on scalp	Primary healing	No headaches, no fits since September, 1941; good cosmetic result; no sedatives; residual paresis of right hand; continuous work, bone graft intact (Fig. 17), February, 1945	Satisfactory
18	F	55	35 yr.; as a child; undefined injury; right frontal; craniectomy for adhesions, 5 years; removal of cyst from brain; celluloid graft inserted	1 yr.; severe throbbing frontal and occipital headaches; neurosis; tender depressed scar; consistently high intracranial pressure of 220 mm.	Slight compression of anterior part of right lateral ventricle; cortical atrophy	February, 1944; removal of two plates of celluloid and "cyst" between them; evacuation of shallow cyst deep to false dura; ilium graft 3 cm. in diameter	Primary healing, after evacuation hematoma	Immediate relief of severe headaches and throbbing sensation; traced for only four months	Relieved

19	M	13 yr.; fall 20 feet off balcony; compound depressed fracture, cerebral laceration, and hemorrhage; immediate operation	5 yr.; Jacksonian fits; worse with service in R.A.A.F.; homonymous quadrantic defects in visual fields	Huge diverticulum from right lateral ventricle to reach site of irregular and depressed fracture; scarred cortex only few millimeters in depth (Figs. 18 & 19)	May, 1944; excision of displaced fragment of bone and cerebral scar; ependyma of left ventricle intact; dura repaired with fascia from external oblique muscle; ilium graft 4 by 3 cm.	Primary healing; some reactionary hemorrhage from ilium wound	No major fits; three minor uncertain "turns," but nil since, on light sedation; graft intact after nine months (Fig. 20); continuous work, February, 1945	Satisfactory
20	M	6 yr.; motor car accident; depressed fracture and cerebral laceration; right parietal; two operations	6 yr.; headaches; left hemiplegia, with severe degree of flexor contraction of left hand and forearm; 2 yr., fits since fall from mast of ship, increasing to status epilepticus	Large smooth diverticulum from anterior horn and body of right ventricle; brain scar 2 cm. in depth	August, 1944; removal large irregular fragment; excision of brain scar; dura repaired with fascia lata; outer table of frontal replaced as graft	Primary healing	Without sedatives, fits recurred, but none for three months on sedation; remarkable improvement in hemiplegia and use of left hand, February, 1945	Relieved

Note: During the interval between Cases 17 and 18, the author was on full-time military service with the Australian Imperial Force.

- (3) Feelings of discomfort, pulsation, and throbbing at the site of the defect, usually associated with cerebral hernia and changes of weather
- (4) The need for protection against further injury to the brain, associated with certain occupations and sports
- (5) Unsightly cosmetic defects causing an inferiority complex

#### CONTRAINDICATIONS

With the advent of the sulfonamides and penicillin, there are now few local contraindications for cranioplasty; but, if the original wound has been infected, and if there remain indriven bone fragments and foreign bodies, a period of at least three months from the time the wound has healed should be allowed to elapse before grafting is attempted.



Fig 1 (Case 2) —Lateral roentgenogram taken before the insertion of the rhum graft in May, 1932

#### ANALYSIS OF CASES

In support of the foregoing contentions, a series of 20 consecutive cases with 21 grafts is submitted. Details of these cases are shown in Table I. As might be expected, there were 19 men and only 1 woman. Excluding the woman their ages varied from 6 to 37 years, the average being 20 years. The various regions of the skull were affected as follows: frontal, 8 cases; parietal, 8 cases; temporal, 3 cases; occipital, 1 case

The onset of symptoms and signs for which relief was sought varied from three months to nineteen years after the trauma; operation was undertaken

from three months to sixteen years after their onset, for the following reasons: fits, 13 cases; headaches, 8 cases; hernia cerebri, 4 cases; hemiplegia, 3 cases; neurosis, 2 cases; cosmetic defects, 2 cases; protection, 2 cases.

In 16 cases, the dura mater and/or brain had been damaged. In 10 of them, encephalography demonstrated the presence of a cerebral cicatrix with traction diverticulum for the underlying lateral ventricle. In all these cases, excision of the cicatrix with its surrounding area of gliosis was performed as far as was practicable (without producing further loss of function) and the dura mater reconstituted, prior to the fixation of the graft.

In 3 cases, the repairs and the grafting were done at separate operations, and in 1 patient (Case 10) a second graft had to be inserted where cadaver bone had been absorbed. The inner table of the ilium bone was used 14 times, cadaver skull 5 times, and autogenous skull 2 times. In 3 cases, free grafts of fascia were needed to repair the dura mater.



Fig. 2 (Case 2).—Lateral roentgenogram taken in February, 1945, nearly thirteen years after the first graft (Fig. 1), showing a good deal of irregular absorption of the ilium graft.

#### DISCUSSION

Some of the cases presented are worthy of special comment, especially Case 5. This patient sustained an injury in the left frontal region and orbit, when a heavy hammer fell 120 feet down the shaft of a mine in which he was working. Primary operation and débridement were performed at a country hospital, and a very satisfactory recovery took place, considering the severity of the trauma. When seen about eight months later, however, the patient complained of headaches and some slight disability with speech and urinary con-

trol; he had had one major epileptic fit. He presented an extraordinarily bad cosmetic appearance (Figs. 3 and 4). He could not voluntarily open the left eyelids, but on separating them the eyeball was seen displaced downward into the antrum. The extent of the damage to the skull and orbit and the indriven fragments can be seen in the roentgenograms (Figs. 5 and 6).

At the operation, alarming extradural hemorrhage was encountered when removal of one of these fragments was attempted. It probably came from the sphenoparietal sinus, and was controlled temporarily by packing with gauze. Following a parlous convalescence, a satisfactory cosmetic result was obtained. Only two fits occurred during the next three years; in a letter written in December, 1944, he stated he was symptom free and working strenuously as an axman in a pine forest.



Fig 3

Fig 4

Fig 3 (Case 5) —Front view, showing the deformity of the left frontal region and orbit  
 Fig 4 (Case 5) —View of the left side

Another patient (Case 10), in addition to fits, also had a bad cosmetic result after injury. His appearance was almost identical with that of the patient shown in Fig 3 of the article by Grant and Norcross<sup>1</sup> (1939). Following removal of several indriven fragments of bone, foreign bodies (dirt), and an extensive area of gliosis, the gap in his skull was filled in with a large piece of bone, removed some time before from a patient with an inoperable brain tumor (Fig. 12). No further fits or headaches occurred, and two years later he enlisted in the Royal Australian Engineers A I F, sailing for the Middle East in



Fig. 5.

Fig. 5 (Case 5).—Anteroposterior roentgenogram showing area of missing bone and indriven fragments.

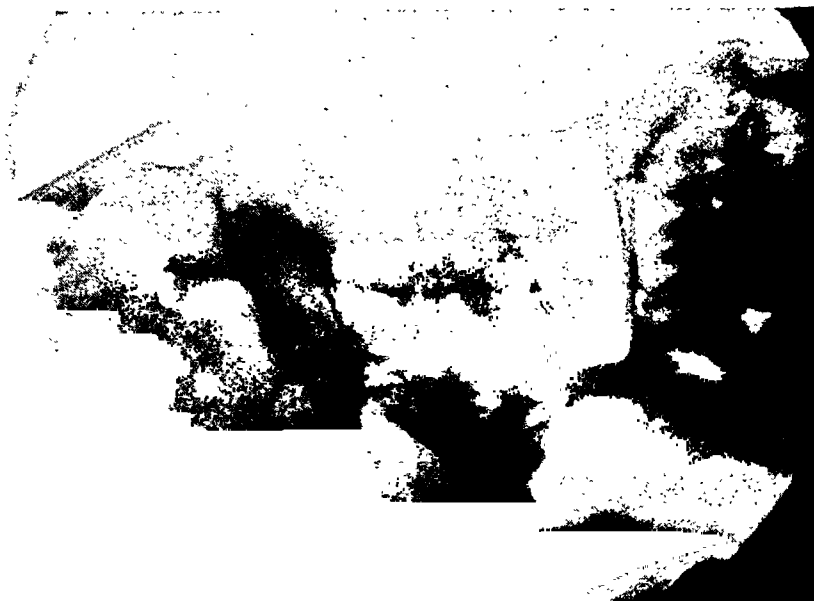


Fig. 6.

Fig. 6 (Case 5).—Lateral view of the facial bones showing the left eye inside the left antrum.



Fig. 7 (Case 8).—Lateral roentgenogram showing the large cadaver graft, April, 1940, shortly after its insertion.



Fig. 8 (Case 8).—Lateral roentgenogram taken in December, 1944, showing only a very slight amount of absorption after nearly five years.

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Fig. 9 (Case 9).—Lateral roentgenogram taken in March, 1940, two years after the insertion of the outer table of a large fragment of the skull as a graft in April, 1938.

Fig. 10 (Case 9).—Lateral roentgenogram taken in December, 1944, showing that there has been practically no absorption of the outer table graft, and that bony union has occurred with the skull in places.





Fig. 11 (Case 10).—Encephalogram taken in December, 1941, showing the large diverticulum from the anterior horn of the right lateral ventricle, which re-formed after the operation in 1938.



Fig. 12 (Case 10).—Lateral roentgenogram showing the cadaver graft in position shortly after its insertion in November, 1938.



FIG. 13 (Case 10).—Lateral roentgenogram taken in December, 1944, showing extensive absorption of the cadaver graft after six years.



FIG. 14 (Case 10).—Lateral roentgenogram showing the ilium graft wired in position, January, 1945.

March, 1940. After taking part in the first Libyan Campaign in 1941, the fits recurred with gradually increasing frequency and severity; he was repatriated and discharged from the Army in 1942. When he was re-examined in December, 1944, the fits were occurring about three times a week. The grafted area felt very irregular and was tender. A roentgenogram (Fig. 13) showed that practically the whole of the graft had been absorbed. The traction diverticulum from the right lateral ventricle was still demonstrable by encephalogram (Fig. 11). The remains of the cadaver graft were removed, together with some additional fragments of displaced bone, and a graft from the ilium was wired in place (Fig. 14). It is too early to predict the final outcome but while the patient was under sedation no fits had occurred for one month after operation.



Fig. 15 (Case 12).—Lateral roentgenogram showing complete absorption of a cadaver graft inserted nearly six years previously. The roentgenogram taken shortly after the insertion of the graft has been lost.

Case 18 (the only woman patient in the series) was of interest because of the length of time the headaches had been present. The nature of the original injury which occurred in childhood could not be determined nor the pathology (if any) for which the first operation was done in the country thirty-five years before. Two celluloid grafts had been inserted at a second operation, elsewhere, six years before, but headaches had recurred within a few months. Subsequently, some regeneration or overgrowth of bone occurred around the edges of the gap in the skull, and at the third operation, one year before, a collection of fluid, enclosed in a smooth adventitious sac, was discovered between the two layers of celluloid. Removal of the celluloid plates, the "cyst," and the new



Fig. 16 (Case 14).—Lateral roentgenogram showing only patchy absorption of cadaver graft inserted five years previously.



Fig. 17 (Case 17).—Lateral roentgenogram taken nearly five years after the insertion of an ilium graft (February, 1945), showing that there has been little absorption and that bony union has occurred.



Fig. 18 (Case 19).—Anteroposterior encephalogram showing the extent of the diverticulum from the right lateral ventricle, almost reaching the site of the fracture.



Fig. 19 (Case 19).—Posteroanterior encephalogram taken with the patient sitting up, to show the upper and outer limits of the diverticulum.

bone formation, and evacuation of a collection of fluid deep to the inner layer of celluloid, relieved the severe headaches, but sufficient time has not yet elapsed for adequate follow-up.

The encephalograms accompanying Case 19 (Figs. 18 and 19) show the extreme degree to which a traction diverticulum from a ventricle may extend. In this patient, the scarred cortex was only a few millimeters thick, but it was possible to dissect it off the ependyma of the diverticulum and leave the latter intact. The insertion of a graft from the patient's ilium (Fig. 20) has relieved the major fits. Three petit mal attacks with visual hallucinations occurred when sedation was stopped too soon. He has, however, been able to continue his work in mechanical engineering.



Fig. 20 (Case 19) —Lateral roentgenogram taken in February, 1945, showing the ilium graft wired into position nine months previously. There has been no absorption and bony union is seen to be occurring.

*Complications* were few. In three patients, infection occurred in the wound of the ilium and did not settle down until several large pieces of Horsley's wax had been evacuated. More careful preparation and storage of the wax, and a less liberal application to the diploic surface of the ilium eliminated this trouble.

In one patient (Case 2) in whom part of the large graft contained the whole thickness of the ilium, during a nocturnal fit one month after operation, a fracture of the ilium was caused by muscular violence. Outward and downward displacement of the fragment was produced by the action of the gluteal muscles. It was replaced by manipulation and kept in place with a plaster cast. After six weeks firm union and a satisfactory result occurred.

The only death in the series was due to a streptococcal infection of a hematoma under the scalp flap. Subsequently, a secondary infection with a

hemolytic *Staphylococcus aureus* also took place. Sulfanilamide and sulapyridine were both administered early, but, in the light of more recent knowledge, the initial dosage was probably inadequate, and the organisms became sulfonamide resistant. In spite of these drugs and removal of the graft, the infection spread to the meninges and to the ependyma of the ventricle whose diverticulum had been opened into widely, with a fatal result about four weeks after operation. The graft itself, though from a cadaver bone, was not incriminated.

Unusual complications occurred in Case 7, not directly concerned with the bone grafting. About one year after the second operation, and associated with an attack of furunculosis, the patient was found to be suffering from diabetes mellitus which could be controlled only with large doses of insulin. As improvement occurred, several hypoglycemic episodes followed, during one of which he had a violent fit and fell downstairs. Some weeks later, a kyphosis was noted in the thoracic region, and compression fractures of the bodies of fourth, fifth, and sixth thoracic vertebrae were discovered in a roentgenogram of the spine. In July, 1942, he died of diabetes mellitus.

#### RESULTS

In eleven patients (55 per cent) "satisfactory" results have been obtained in that, for periods from nine months to thirteen years after operation, they have been symptom free and at continuous work. Of these patients, six had had epileptiform fits. Thus, 46 per cent of the patients suffering from traumatic epilepsy appear to have been cured.

Five patients, of whom four had had fits, were classified as "relieved," in that their symptoms and fits occurred with less frequency and severity. In two patients (Cases 7 and 15) no relief of fits occurred after depressed fragments of bone, foreign bodies, and adhesions were merely dealt with; the brain scars were excised later. Relief was then afforded the former. Unfortunately, the latter died.

Two patients had been classified as "unsatisfactory." In one (Case 10) the fits recurred three years after insertion of a cadaver graft, but if the second operation with ilium graft is more successful, he may be upgraded later. In another (Case 12), after one year's freedom, fits recurred upon cessation of sedation, but he was able to serve three years in the Armed Forces. The graft in this case was also composed of cadaver bone, and a second operation to insert a graft from the ilium bone is contemplated. Finally, in one patient who had not had fits, follow-up was only for a few months and has not been classified.

#### FATE OF THE GRAFT

Where cadaver bone has been used, varying degrees of absorption of the graft have taken place. In Case 12, the roentgenogram (Fig. 15) taken nearly six years after operation does not show any radiologic evidence of the graft, which appears to have been completely absorbed. The defect, however, felt quite solid and was not tender. In Case 10, absorption was extensive, but not quite complete in six years (Figs. 12 and 13). There was much less absorption in Case

14, as can be seen from the roentgenogram (Fig. 16) taken five years afterward; in Case 8 only a few small areas of absorption were noted after nearly five years (Figs. 7 and 8).

The fate of the ilium grafts has been more satisfactory. In Case 17, the roentgenogram (Fig. 17) taken nearly five years after operation shows that the graft is practically intact and that bony union has occurred at many places around the periphery. In Case 2, although some absorption has taken place during the thirteen years which elapsed (Fig. 2), the clinical and cosmetic result has been satisfactory. In Case 19, after a period of nine months, the graft looks intact and bony union has already occurred (Fig. 20). Other patients have been traced by letter, and their clinical results are uniformly good. Furthermore, in Case 7, where a second operation was performed twenty months after the graft, for excision of the brain scar, the graft was found intact, and bony union had occurred between it and the skull, except at two small areas. Thus, the chances of survival of ilium grafts appear to be excellent.

Similarly, where the outer table of a large fragment of the skull was used (in Case 9), the graft has undergone very little change (if any) after six years (Figs. 9 and 10), so that this form of grafting also appears to be satisfactory, when available.

#### SUMMARY

- 1 The sequelae of cranial defects, both organic and psychologic, are discussed, and reasons for their repair are given.

2. Some historic aspects of the various methods of grafting are referred to, and attention drawn to the different sources of grafts (a) from bones, both autogenous and homogenous, and (b) from inorganic materials, such as celluloid, metals, and plastics.

3. The advantages of using the inner table of the ilium bone over other bones and various inorganic substances are pointed out.

4. Indications for bone grafting to the skull are given and important points in the operative technique and its scope, are described.

5. Table I is submitted, giving details of a series of 20 consecutive patients treated with 21 grafts. In 16 patients, laceration of the dura mater and/or brain had occurred; in 10 patients, brain scar and ventricular diverticulum had developed; 13 patients had suffered major epileptiform fits. Special comment is made upon the unusual features of some of the cases.

6. The inner table of the patient's ilium was used on 14 occasions, and the outer table of the skull, 2 times. Cadaver grafts were used in the remainder. On 3 occasions, a free graft of fascia was used to repair or replace damaged dura mater.

7. The follow-up results for periods from thirteen years to nine months are presented: 11 cases have been classified as satisfactory; 5 as relieved, 3 as unsatisfactory" (including one death), and 1 was not traced long enough to be classified.

8. Of the 13 patients who had fits, 6 had been regarded as cured, and 4 as relieved.



The assistance of the various resident medical officers and anesthetists who performed their duties so ably in these long and often tedious operations during the period under review is gratefully acknowledged.

The Australian Broadcasting Commission and the Sydney Press helped materially in tracing some of the patients. Mr. Woodward Smith of the Department of Medical Artistry, University of Sydney, took the portraits used in Case 5, and Mr. J. J. Fallon of Sydney kindly made the prints from the various roentgenograms reproduced.

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## CEPHALHEMATOMA DEFORMANS

### LATE DEVELOPMENTS OF INFANTILE CEPHALHEMATOMA

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HEAD injuries acquired before, during, and just after birth, in infancy and in childhood, are now generally recognized as important causes of severe cranial and cerebral lesions leading to mental abnormalities, epilepsy, mono-, hemi- or diplegia, blindness, or deafness.

The sequelae of infantile head injuries are somewhat different from cranial and intracranial post-traumatic lesions in adults; they are as follows:

1. Fractures of the infantile skull may not heal by bony union; on the contrary, the dehiscence between the margins of the fracture may enlarge, thus producing a considerable cranial defect after some years. Probably this is due to general or local increase of the intracranial pressure (*meningocele spuria traumatica Billroth; hernia cerebri traumatica*).

2. Subpericranial and extradural collections of blood (*cephalhaematoma neonatorum* and *infantum*) sometimes produce in their late stages cystic cavities, osseous shells, or tumorlike hyperostosis of the cranial walls.

3. An extensive ossification occasionally takes place inside organized subdural hematomas following infantile head injuries.

4. Cerebral or meningeal hemorrhages of early childhood often cause diffuse or localized shrinkage of the brain (traumatic porencephaly and microgyria) with consequent enlargement of the ventricles or formation of cysts containing cerebrospinal fluid.

5. Uni- or bilateral micro- or hydrocephaly, generalized or localized thickening or thinning of the cranial walls may develop in childhood due to post-traumatic scar or cyst formation of the intracranial contents.

6. It is not infrequent that characteristic calcifications called "brainstones" are formed during childhood in traumatic scars of the brain.

Roentgenologic examinations afford the best opportunity to study the development of the post-traumatic cranial lesions mentioned. The roentgen findings are often significant in cases where the history and clinical examinations are not very helpful for diagnosis. Dandy's encephalographic method is of outstanding importance for the detection of intracranial abnormalities due to infantile head injuries.

In this paper we are dealing with the clinical state and the roentgen appearance of the late developments of infantile cephalhematoma. It is well known that infantile cephalhematoma persists for weeks or months and then, as a rule, completely disappears. Occasionally in the later stages hyperostosis or cyst formation of the cranial walls takes place; to this peculiar organization of cephalhematoma Recklinghausen gave the name *osteitis fibrosa cystica*. Choyce stated: "An ossified haematoma might simulate leontiasis or tumour of

the skull, but will be distinguishable in a skiagram and by palpation, if, as like ossification is incomplete over the summit of the swelling" Chorobski and Davis<sup>2</sup> gave a detailed review of clinical and surgical experiences regard cephalhematomas. Schuller<sup>3</sup> described x-ray findings in a case of cephalhematoma frontale.

In the case reports are presented clinical histories and x-ray findings in 1 cases with diagnoses of late development of infantile cephalhematoma.



Fig 1 (Case 1)—Lateral roentgenogram of the right side of the skull showing hyperostosis right frontal area

#### CASE REPORTS

CASE 1—Miss M, aged 27 years, complained of occasional headaches for three years. When 9 years old she was hit on the head by a falling blackboard; a swelling which persisted since developed quickly on the right side of the forehead. On examination the right side of the forehead, mainly in the supraorbital region, and the adjacent temporal area were found to be prominent, the right eyeball stood lower than the left. The swelling could easily be moved over the smooth, nontender prominence. There were no objective subjective murmurs. Smell and eyesight were normal.

Radiograph of the skull (Fig 1) showed thickening of the right side of the forehead up to 16 cm., corresponding to the major part of the vertical plate of the frontal bone. A sharp outline could be seen between the thickened and neighboring normal part of the cranium. The diploe of the thickened area appeared partly normal, partly raised, and contained scattered dense islands 2 to 5 mm. in diameter. The internal lamina was thin and dense, the external lamina well outlined but thinned or absent over the summit of the bulge.

The frontal sinus was absent on the right side; the left frontal sinus was normally developed as were the other sinuses on both sides. The horizontal plate of the frontal bone on the right side was thickened up to 12 mm. and had a dense structure; it formed a flattened roof over the right orbit, the level of which was 1 cm. below the level of the left orbital roof.

CASE 2.\*—Mrs. B., aged 54 years, was sent to the Melbourne Radiological Clinic for x-ray examination of the chest and paranasal sinuses. An abnormal appearance of the frontal bone was detected. Clinical examination showed a tumorlike prominence in the right frontoparietal region. The swelling followed a fall on the floor when the patient was some weeks old; it had never caused trouble. X-ray examination of the cranium (Figs. 2 and 3) revealed the following details: The medial part of the right parietal bone and the vertical

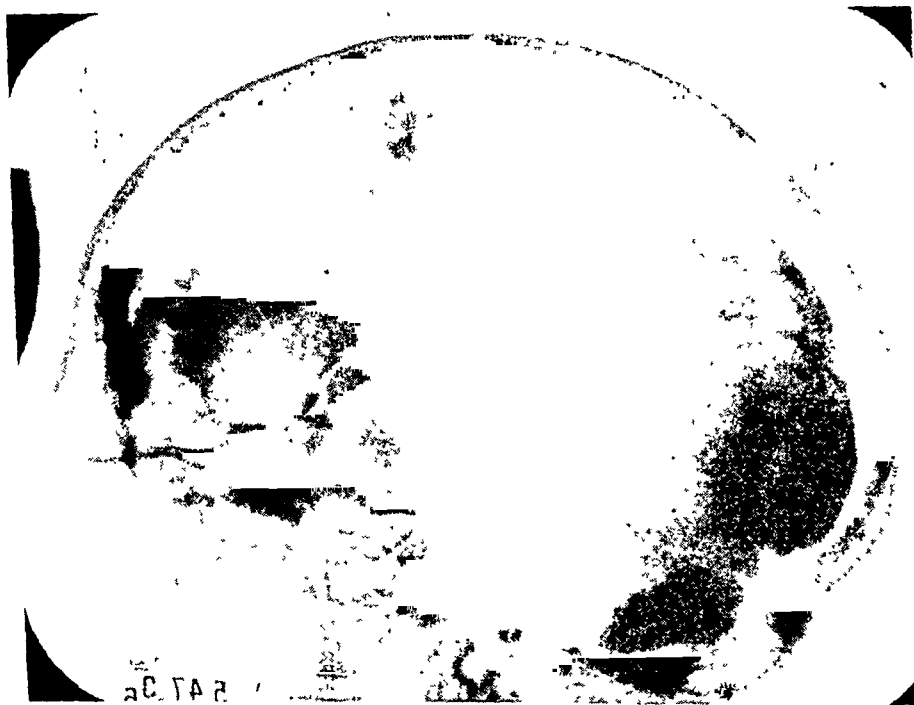


Fig. 2 (Case 2).—Lateral roentgenogram of the right side of the skull showing hyperostosis of right frontal area.

portion of the right frontal bone were thickened. The appearance of the internal and external laminae of the thickened area was not much different from the normal side. The diploe had a mottled appearance due to the presence of osteoporotic and sclerotic islands. No sharp outline could be seen between the mottled area and the normal cranium. The frontal sinus was absent on the right side; it was of medium size and normal shape on the left side. There was also a pronounced difference between the two halves of the anterior part of the base. The horizontal portion of the frontal bone, the posterior part of the ethmoid, the body, and the lesser wing of the sphenoid were much thicker on the right than on the left side. The roof of the orbit stood on a lower level than on the normal side. The thickened right lesser wing of the sphenoid was of uniform dense structure; the thickened right half of the sphenoidal body and the right posterior ethmoid were partly dense, partly pneumatized. A supraorbital extension of the right ethmoidal cells filled the anterior half of the right horizontal plate of the frontal bone.

\*History and radiographs of this patient through the courtesy of Dr. Stuart Crooks.

In Cases 1 and 2 there was similar roentgen appearance, namely, (1) thickening of the right anterior part of the calvaria presenting a mottled diploetic structure, (2) eburnated hyperostosis of the right anterior part of the base of the skull, (3) an atypical paranasal pneumatization on the right side.



Fig. 3 (Case 2).—Posteroanterior view showing hyperostosis of right side.

CASE 3.—Mrs. O'D., aged 72 years, was sent to the x-ray department of St. Vincent's Hospital for examination of a cranial deformity. The patient herself did not want this examination as she had never been inconvenienced by the cranial deformity. In her early childhood she had been hit on the head by an axe; a cranial deformity developed after the injury. The photograph of the patient (Fig. 4) shows an asymmetrical prominence of the forehead and the naso orbital region; both eyeballs appear displaced laterally, the left one more so than right. Enlarged veins could be seen on the skin covering the left frontotemporal prominence. The left eyebrow was elevated. On palpation the bulge was resistant like bone and not tender. The skin could be easily folded over the bulge.

Radiograph (Fig. 5) showed an enormous thickening of the anterior part of the cranial wall; the tumorlike prominence was mainly eccentric and more pronounced on the left side. The largest diameter of the thickening was about 6 cm. Lamina externa and interna were well outlined and smooth. The space between the two laminae contained cystic cavities, normal and porotic diploe, and numerous islands of dense bone, some of which looked like eburnated sequestra. No frontal sinuses could be seen. In the base of the skull the pos-



Fig. 4 (Case 3) —Photograph showing deformity of face and skull'

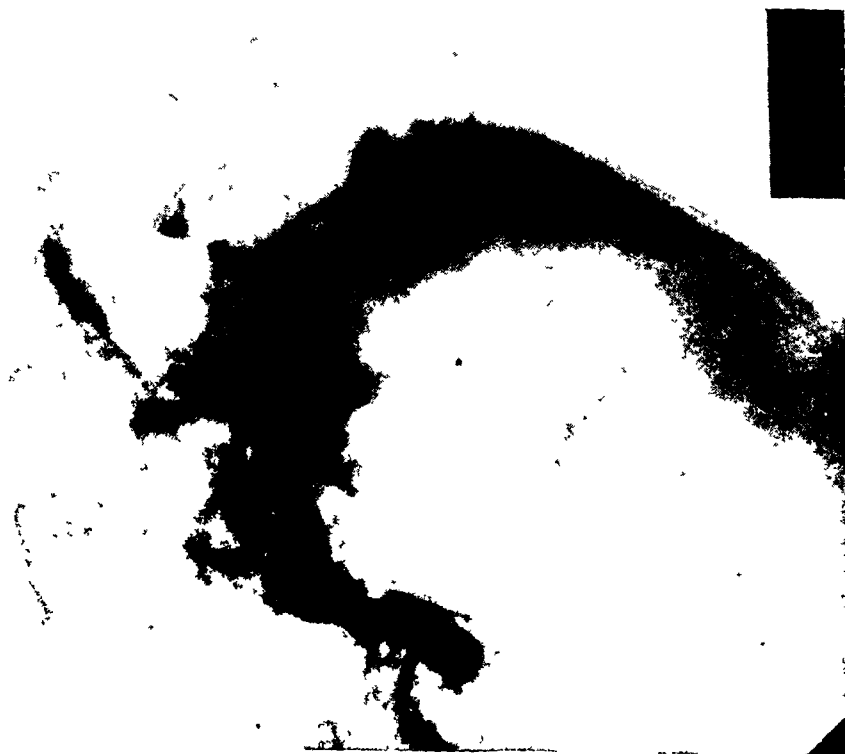


Fig. 5 (Case 3).—Lateral roentgenogram of the right side of the skull showing extreme deformity and hyperostosis.

terior part of the ethmoid and the anterior part of the sphenoidal body presented an enormous enlargement up to 6 cm in the transverse diameter between the orbital cavities (hyper telorism). The structure of the enlarged parts was dense on the left side; pneumatization of the ethmoid and sphenoid was present on the right side. The great wing and the pterygoid process on the left side were thickened and dense. The horizontal parts of the frontal bone had a peculiar appearance: Profile radiographs showed the outlines of the cranial and orbital plates distinctly on the right side; the two plates diverged from behind forward at an angle of 45 degrees and were separated from each other by spongy bone; on the left side the horizontal portion of the frontal bone appeared thicker and denser than on the right side; its orbital plate was indistinctly outlined.



Fig 6 (Case 4) —Lateral roentgenogram of the right side of the skull showing marked hyperostosis

In Case 3 the extent of the asymmetrical hyperostosis occupying the fronto-temporal region and the anterior basal part of the skull was enormous. The roentgen appearance of the cranial deformity was bizarre and offered some difficulty of explanation. Nevertheless, the peculiar type of the deformity and its structural abnormalities could be well interpreted by comparison with the findings in Cases 1 and 2, especially with regard to the mottled appearance of

the diploetic hyperostosis of the calvaria and the dense hyperostosis of the base. An excessive degree of hypertelorism was present in this case: the orbital cavities were 6 cm. apart. Pneumatization of the frontal, ethmoidal, and sphenoidal bones was absent on the left and poorly developed on the right half of the skull.

CASE 4.—Mr. R., aged 71 years, presented a pronounced deformity of the forehead, noticed since early childhood; it did not cause any trouble. X-ray examination of the head (Fig. 6) showed thickening of the anterior half of the cranium and of the base of the skull. The hyperostosis was more pronounced on the right side. No paranasal sinuses were present on the right side, but there were large ones on the left. The structure of the hyperostosis was similar to that of Case 3.

The comment given on Case 4, when published by one of us (A. S.)<sup>3</sup> in 1940, was as follows:

“With regard to the history of the case, especially the presence of the deformity since early childhood and the absence of clinical symptoms during the whole life, the most probable diagnosis is: Cephalhaematoma.



Fig. 7 (Case 5).—Photograph showing exophthalmos and deformity.

“We can imagine that in early childhood a large traumatic haematoma elevated the outer periosteum of the anterior half of the skull. Later on, the wall of the haematoma was ossified, forming a cystic cavitation. Inside the blood clot different types of osseous structure have developed, spongy bone, nodules and ridges, but especially a most unusual looking new growth-like hypertrophy of the walls of the rudimentary sinuses.”



CASE 5.\*—Miss P., aged 20 years, complained of double vision and prominence of the left eye seven weeks before admission to the Cancer Hospital, London. Three weeks later an aching pain developed in the left supraorbital and temporal region. This region was injured in childhood by a cricket ball. The injured area of the skull had since been prominent. During the four weeks previous to admission to the hospital the swelling had increased in size. After admission the pain disappeared and the swelling became smaller after rest in bed.

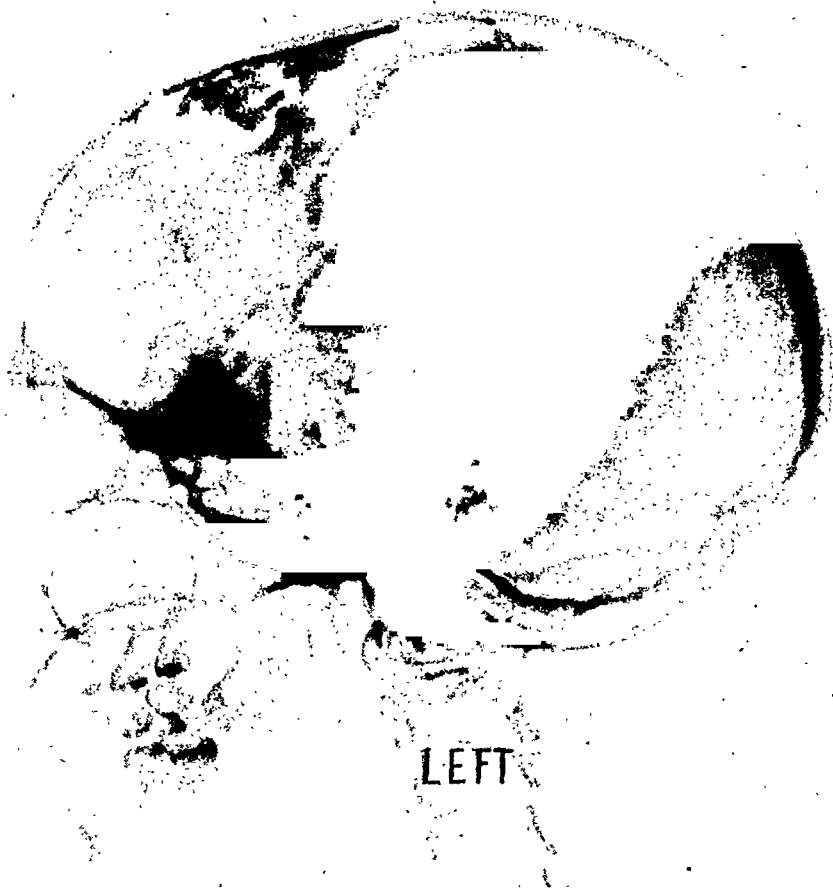


FIG. 8 (Case 5).—Lateral roentgenogram of the left side of the skull showing large defects and hyperostosis.

Examination showed a diffuse enlargement of the left frontal and temporal region (Fig. 7) and a small shallow depression about one inch in diameter above the left supra-orbital margin. The skin over the whole region was normal, neither fixed nor tender. The bone felt soft like a fetal skull at the site of the shallow depression mentioned previously. The left eyeball was displaced forward and downward. The lacrimal gland felt hard and was pushed forward. The actual movements of the eye were normal apart from disability due to alteration in position. Vision was normal; there was no pulsation of the eyeball; no bruit was audible.

Blood and urine examinations were normal. Wassermann test was negative, *inner* organs were normal, and radiographs of the skeleton negative.

\*Clinical history of this patient, photographs, and radiographs were sent to one of us (A. S.) by the late Professor I. M. Woodburn Morrison.

A small piece of bone was removed from the left frontal region at the periphery of the swelling. The trephine plug was examined by the pathologist. He reported that the associated features of the histology of the specimens and the failure to detect any trace of a neoplastic or granulomatous process suggested that the condition was primarily pressure necrosis of the bone, probably of traumatic origin, resulting in supracranial or intracortical hemorrhage which failed to organize and induced a rarefying osteitis in the neighboring bone; the vascularity of the loose connective tissue filling the spaces would be liable to increase the absorption of bone; and to favor hemorrhages. Massive hemorrhage into coalescing residual cysts following such hematomata would tend to occur.

Radiographic examination of the skull (Fig. 8) showed the following details: The bulge of the left forehead was caused by thickening of the vertical portion of the frontal bone. A large defect of the bone was present corresponding to the depression in the left supraorbital region. The defect measured two and one-half inches in the vertical and two inches in the transverse diameters; the outline of the defect was irregular. The structure of the surrounding thickened part of the frontal squama appeared diploetic and mottled by spotted sclerosis. Frontal sinuses were wanting. On the base of the skull there were marked changes in the walls of the left anterior and middle fossae. The roof of the left orbit was absent. Its defect appeared to be continuous with the large defect in the vertical portion of the frontal bone. The greater and lesser wings of the sphenoid on the left side were thickened and of dense structure. The left half of the sphenoidal body was not pneumatized; the sphenoidal sinus on the right side was well developed.

In Case 5 are shown the characters of unilateral frontal hyperostosis similar to those in Cases 1 and 2. Case 5 varies from the other two in that there was a large defect in the central portion of the hyperostosis. Parts of the vertical as well as the horizontal plate of the frontal bone were destroyed. The destruction was probably caused by a recent hemorrhage inside the hyperostosis.

#### DISCUSSION

The histories, the clinical signs, and the radiographs of five adult patients have been described, showing similar and characteristic features:

1. A history with origin in infancy or childhood (a cranial injury is mentioned as the cause in four of the five cases)
2. A peculiar type of bulging of the forehead, more pronounced on one side
3. A circumscribed cranial hyperostosis presenting an unusual and bizarre structure

No sign or symptom of intracranial or ocular disorder was present in Cases 1 to 4. The deformities of the head which endured from youth to adult life did not worry the patients. The ages of the four patients when examined were 72, 71, 54, and 27 years.

One patient (Case 5) entered the hospital because of headaches and protrusion of the eyeball suddenly at the age of 20 years. A defect of the frontal bone in the center of the hyperostotic area was detected by clinical and radiographic examinations. This defect was probably due to fresh hemorrhage. The sudden onset of symptoms can be attributed to pressure by the hematoma. This explanation is supported by the result of the biopsy.

One patient (Case 4) was a man, the others were women.

The roentgen appearance of the peculiar type of circumscribed hyperostosis can be summed up as follows: The calvaria and the base of the anterior part of the skull are involved, mainly on one side. These parts are thickened considerably, up to 6 cm. in one case. The thickening is mainly eccentric, its ill-

defined edges merge gradually into the normal neighboring bone. The structure of the hyperostosis is not uniform; diploe lined by thin external and internal laminae prevails in the thickened calvaria, eburnated hyperostosis in the basal area. One may find osteoporosis, osteosclerosis (similar to the well-known structure of the calvaria in Paget's osteitis deformans), cystic cavities, and bony fragments resembling sequestra inside the bony swelling of the calvaria. Sometimes paranasal sinuses are not developed on the diseased side; if they are, their shape is atypical.

None of these patients required operative treatment.

We propose for the cranial deformities represented by the five cases described here the name "Cephalhematoma deformans."

The pathogenesis of cephalhematoma deformans can be explained as follows: Early stages of infantile cephalhematoma occasionally show new formation of bone along the elevated pericranium, along the displaced dura mater, and inside the swelling. The newly formed bone may completely disappear; rarely it persists and grows *pari passu* with the growth of the normal part of the skull. Osteoporosis or osteosclerosis and formation of sequestra or cysts may develop inside the swelling. Paranasal pneumatization is absent or atypical. Fresh hemorrhage may occur and partially destroy the swelling.

Differential diagnosis must eliminate various types of cranial thickening: osteoma, chondroma, sarcoma, leontiasis ossea, meningiomahyperostosis, hyperostosis combined with facial nevi and angiomas, syphilitic hyperostosis, hyperostotic type of xanthomatosis, hyperostosis in neurofibromatosis Recklinghausen, osteitis fibrosa cystica Recklinghausen, Albright's disease, hyperostotic oxycephaly, hypertelorismus Greig, mucocle of the paranasal sinuses, cholesteatoma of the cranial bones, cholesteatoma of the paranasal sinuses.

#### SUMMARY

This paper deals with the late developments of infantile cephalhematoma.

Five patients, one man and the four women, at the ages of 20, 27, 54, 71, and 72 years, respectively, showed a peculiar type of cranial deformity—a unilateral bulging of the anterior part of the skull.

It was unusual for the patients to complain of symptoms referable to the cranial abnormality.

X-ray examination revealed an extensive hyperostosis as the basis of the deformity. The anterior part of the skull was involved. The structure of the hyperostosis was not uniform; diploetic hyperostosis prevailed in the calvaria, eburnated hyperostosis in the basal area; osteoporosis and sclerotic islands, large sequestrum-like fragments of bone and sharply outlined cavities inside the diploe were characteristic features of the structure. Pneumatization was wanting or atypical in the hyperostotic area.

The name cephalhematoma deformans seems adequate for this peculiar type of hyperostosis.

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## CONCUSSION AND CONTUSION

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THE only way in which mechanical forces have been shown to cause a reversible block of nerve conduction is by straining nerve fibers to a critical extent. Romanes recorded a condition similar to concussion in medusae which lay on an anvil while it was repeatedly struck. This does not happen with slugs and snails even when immersed in a water bath with the anvil as the floor. Even with supersonic vibrations which one would expect to be the ideal system of producing commotion in cells, the effect appears to result from bubbling, producing local stretching, or from heating.

With this fact that strain is the only mechanical method of producing reversible nerve block as a basis, we can now consider the present knowledge of the mechanism of production of reversible and irreversible injury of neuraxial tissue by mechanical forces. Denny-Brown and Russell showed that if the head is allowed to move freely under the impressed force the threshold for injury of a given degree is lower than when this is resisted by a counterforce, that is, the energy application for concussion is less when the applied force produces free acceleration of the head than when it produces deformation of the head only.

The following are possible results of applying force to the free stationary head:

1. A linear acceleration of the whole skull and its contents in the line of the applied force.

2. An angular acceleration of the whole skull and its contents about an axis within or without the cranial boundaries.

3. Distortion of the skull with production in the rigid resilient bony structure of longitudinal and transverse waves which are highly damped by the liquid loading of the contents and surroundings.

4. Distortion of the skull with production of general change in pressure within it. With an ellipsoid of revolution bounded by a rigid resilient wall, reduction of the long axis results in a generalized decrease of pressure in the content, and reduction of a short axis results in a generalized increase in pressure.\*

The skull may not, however, behave simply as an ovoid bottle. The curious sliding surface between the squamous temporal and neighboring bones suggests considerably more complex possibilities. There is not at present any mechanism which could be relied upon to register intracranial pressure on impact. That used by Denny-Brown and Russell is completely inadequate.

In most cases of application of force to the skull, the result will be a combination of all these possible changes. The proportion of the applied

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\*This feature of ovoid bodies was pointed out to me by Professor W. A. Osborne.

energy appearing in each change will depend on the velocity (vector), mass, and physical properties of the impinging object and on the physical characters and the spatial relations of the part of the particular skull to which it is applied.

The anatomic attachments of the skull are of the greatest importance. It is always attached to the neck which can be bent but has an axial constituent of great strength, the vertebral column. This is broken up into segments of rigid bone joined by strong but elastic structures, the ligaments; attached to it are masses of viscous liquid material. Thus, a force applied along a line which would produce linear acceleration in an unattached skull may produce an angular acceleration as well as a rectilinear acceleration of the attached skull and the linear acceleration will always bear some relationship to the axis of the neck.

Omitting for the moment the physical changes produced within the skull during acceleration and treating it as moving as a whole it is important that although the skull is joined to the vertebral column by strong but elastic ligaments, the intracranial neuraxis is joined to the spinal cord by the weak spinomedullary junction with an extremely low coefficient of restitution. Denny-Brown and Russell stated that in experimental cats they produced an acceleration from a velocity of 0 up to 28 feet per second in  $\frac{1}{4,000}$  of a second; this is approximately 1,000 g and very improbable. Accepting it as a basis for simple calculations, however, we have also the average weight of the spinal cord of six cats as 7 Gm. If the skull and its contents in their experiments moved directly away from the spinal column the force at the spinomedullary junction due to the inertia of the cord would be approximately 6.2 kg. weight. A very small fraction of this would be sufficient to produce functional impairment of this junction. This analysis can be applied to acceleration not in direct line with the spinal cord by working out the components.

The threshold which Denny-Brown and Russell have stated for the cat is an acceleration from standstill to 28 feet per second in  $\frac{1}{4,000}$  of a second. Actually, neither of these figures was the result of measurement. The final velocity of the head was probably in the neighborhood of 40 per cent of that reported by the authors (see Appendix), that is, the critical final velocity for cats was 11.2 feet per second, not 28 feet per second. The time in which this was produced cannot even be guessed at. To check on the figures, cats were anesthetized by inhalation of ether and suspended from a crossbar by copper wires entered under the planum occipitale at the external protuberance and emerging at the temple after passing deep to the zygomatic process of the temporal bone. The crossbar was allowed to fall on a taut guide wire to a length of piping screwed to a floor joist (Fig. 1). The time of deceleration was not measured but was almost certainly greater than  $\frac{1}{4,000}$  of a second. A fall from 4 feet was sufficient to cause jerking, disorder of respiration, and loss of corneal reflex in five cats. A fall from 5 feet caused death with bleeding at the spinomedullary junction in all but one of six cats. The critical velocity in these cases was therefore about 16 feet per second.

To check whether the distortion at the atlanto-occipital region is the origin of the nervous lesions in these cases, cats were similarly suspended but completely immersed in a can of water. A tracheal cannula and rubber tube gave a respiratory pathway through the side of the can, and the buttocks of the cat rested on the bottom of the can. On dropping this can from a height of as much as 12 feet (terminal velocity, 27 feet per second), no signs of concussion were detected. In this case the time for deceleration was measured with a high-speed moving picture camera (2,300 frames per second) and time

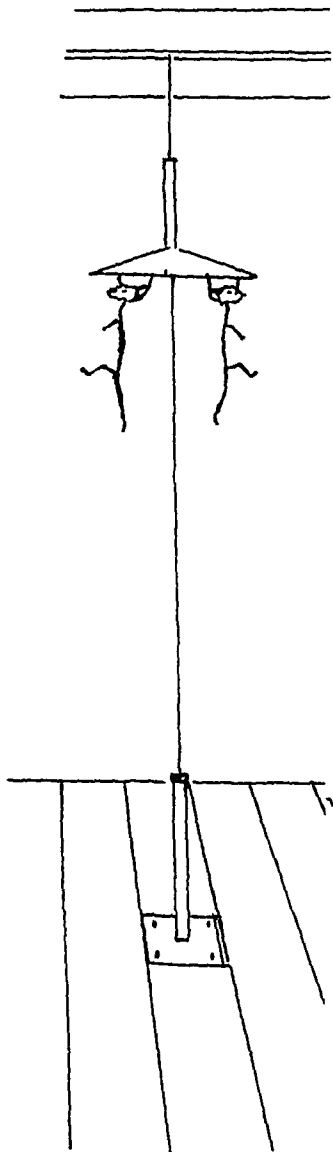





Fig. 1.—General setup for decerebration experiments. The cats are suspended by the skull to the crossbar which falls freely on the taut vertical wire until checked by the vertical stop screwed to the floor.

marker; it was  $\frac{1}{1,600}$  of a second. This deceleration was half as great again as that claimed by Denny-Brown and Russell and probably six times as great as that described in the preceding experiments. In the case reported here, distortion at the atlanto-occipital region was reduced to a minimum and no disturbance of the nervous phenomena resulted.

As to whether such local distortion could result in unconsciousness we have the statement of Foerster<sup>4</sup> that local pressure (that is, distortion) on the neuraxis at this junction produces loss of consciousness more easily than does pressure applied anywhere else. It is thus obvious that acceleration and deceleration cannot be used interchangeably without taking the whole of the condi-

tions into account. Thus, a cat with the head accelerated thus 

is subject to the same forces as a cat decelerated thus 

but not the same as a cat decelerated in this way: 

In this latter system there is bony compression of the cervical vertebrae and the cord tends to invade a fixed volume, subjecting the spinomedullary junction to very little strain. In the former cases the ligaments are stretched and the spinal cord pulls on the spinomedullary junction.

Holbourn has advanced very good reasons for considering that angular acceleration may be a very important factor in causing intracranial damage. Briefly, the argument is that the moment of inertia of a particle of mass " $m$ " at a distance " $r$ " from the axis of rotation equals  $mr^2$ . Thus, if we take the skull (Fig. 2) with an angular acceleration about an axis " $a$ " within the skull, the resistance to acceleration of the two equal particles " $m^1$ " and " $m^2$ " is as  $\frac{(am^1)^2}{(am^2)^2}$ . It is obvious, too, that if the axis of rotation is outside the limit of the skull, for example at " $a^1$ ," the moment of inertia of " $m^3$ " will be greater than that of " $m^4$ ," and therefore a movement of the liquid within the skull will result. The same principle applies as to the movement of fluids in semicircular canals. But the acceleration is being impressed on the viscous liquid contents of the skull by the skull because of its greater rigidity. Consequently, the part of the viscous content nearest to the inner layer of the skull, even though it may have the highest moment of inertia, will accelerate most nearly at the rate of the skull and the succeeding layers will tend to slide on each other. Where there are projections such as the alae pterygoideae there will be maximum distortion and macroscopic damage. But apparently Holbourn was not aware that Ferrari<sup>4</sup> had found that glass-walled chambers when disposed within the cranial content obliquely or perpendicular to the line of acceleration of the head were broken only when within 5 mm. of the inner surface of the skull. Although Ferrari did not analyze this in terms of angular acceleration it would appear to support the interpretation that as a result of angular

acceleration there is a strong shearing of the external layers of the cerebrum on the deeper layers. It is very probable that such a result over a large area of the cerebrum would result in unconsciousness in the milder trauma, and macroscopic damage in the greater trauma.

The third and fourth results of force applied to the head also need consideration. It is very easy to demonstrate with a piezoelectric crystal applied to the external surface of the intact cranium that transverse waves travel round the bony calvarium when the skull is hit (Fig. 3). It is probable that the energy imparted in glancing blows by small masses is dissipated mainly in this form. With sections of the skull as the walls of a ripple tank some idea of the pattern of internal pressure can be gained (Fig. 4). As the pressure waves in the content of the intact skull would all travel at the same speed it is probable that these ripple tank pictures approximate to the real distribution of foci of pressure change in the intact cranium.

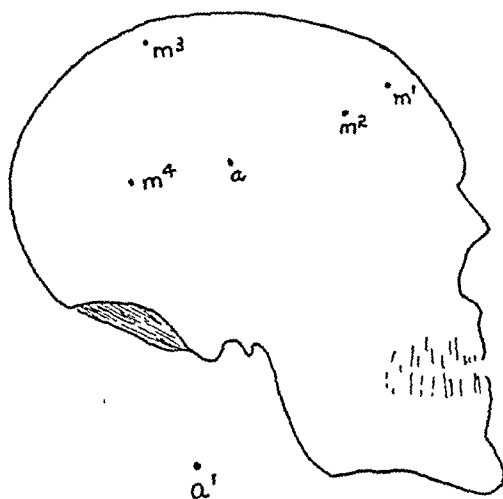


Fig. 2.



Fig. 3.

Fig. 2.—Diagram of skull showing effects of angular acceleration on intracranial contents.

Fig. 3.—Oscillograph trace from piezoelectric crystal on the temporal part of a human skull struck on the occiput, time marker:  $\frac{1}{100}$  sec.

The original premise was that the sole manner of injury of nervous tissue is by shearing of tissue. As Holbourn stated, the intracranial contents, when subjected to increased pressure, are as incompressible as water, but they do not show the same reactions to reduced pressures as does water. The blood contains 20 c.c. of  $O_2$  and approximately 60 c.c. of  $CO_2$  per 100 c.c. of blood. This gas is rapidly released and forms bubbles readily at approximately  $\frac{1}{2}$  atmosphere pressure when of course its volume is doubled. If such a release of gas takes place at a zone of low pressure, shearing of nervous tissue can readily occur. Whether this liberation of gas does in fact occur was tested by placing a blood clot in one end of a glass bottle of elliptical section, the remainder being filled with gelatin which was allowed to set. The side hole was then filled with paraffin and plugged. The end of the bottle opposite to the





Fig. 4.—Ripple tank pictures of various sections of human skull struck in the directions indicated by the arrows. The ripple tank was made by cementing a section of skull 1 inch deep to a glass plate, and filling to  $\frac{3}{4}$  inch with water. The photographs were taken by transmitted light and show the sequence of wave propagation. In series these are sections of horizontal, coronal of middle and posterior fossa, sagittal to side of midline and horizontal.

blood clot was then struck with a heavy rubber tire hammer. Fracture of the blood clot with residual bubbles was observed.

It is evident, therefore, that the three mechanisms mentioned can cause damage to the neuraxis. It would not be safe to conclude, however, that only by such damage does loss of consciousness result. Schmidt has shown that the loss of consciousness in dogs given sublethal doses of cyanide is due to action on the end organs of the carotid and aortic bodies. I have seen a fellow student rendered unconscious by pressure in the carotid sinus area for a duration of only a second or so. Breslauer records loss of consciousness from irritation of the gasserian ganglion in both man and dogs.

#### CONCLUSION

The cause of concussion and contusion is spatial distortion of the elements of the neuraxis. This may occur at the spinomedullary junction when the head is accelerated away from the neck. It may occur in the intracranial contents when the head is rotated (Holbourn). It may result from distortion of the cranium. It may also result from liberation of bubbles from the intracranial blood in areas of reduced pressure.

I wish to thank Dott & Co. for the blowing of special ovoid glass vessels, and Mr. Frank Nicholls for assistance in piezoelectric recording.

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*(See next page for Appendix)*

About one month before, he had developed a voracious appetite, became very thirsty, and extremely sleepy. He had also gained much weight over this period, particularly about the neck. Since then he had suffered from attacks of "phlegm in the throat," which for the last week had troubled him greatly. At times, about one week before, breathing was abnormally rapid.

On March 8, 1944, at 9 A.M., he had a sudden attack in which his face became a high Turkey-red color with a touch of blue, although he was white about the mouth and nose. Hands and feet were blue and cold. A little later he perspired heavily, began to breathe quickly, and became sleepy or semiconscious. Gradually color returned, the entire attack lasting about one hour.

Afterward he was sleepy but could recognize his parents and often asked for food. At 12:30 he had a drink of water and asked for a biscuit, but after two bites he inhaled deeply and began to jerk his limbs, holding his breath for about one minute. At 1:30 P.M. he developed jerking attacks, with hands and feet clenched and eyes deviated, which started on the right hand and passed to the left. For about one-half hour he seemed semiconscious. He was rational at 3 P.M., but still asking for food and drink. At 4:30 he had a slight attack lasting for five minutes, but was semiconscious for ten minutes.

Phenobarbital,  $\frac{1}{4}$  gr. hourly, seemed to relieve him, but all night breathing was very quick and pulse racing.

Next day he was brought from Tasmania to Melbourne by plane. At 7:30 A.M. he was quite conscious and breakfasted on porridge, tea, and toast. On the way to the plane by car he was sufficiently alert to recognize once that the driver was taking the wrong road.

After being in the plane for one-half hour he complained of being hot, and flung his arms about. Phenobarbital was given and he became drowsy.

*Examination.*—On May 8, 1944, examination at 6:30 P.M. disclosed an obese child, flushed and breathing rapidly. Respirations were 50 per minute, pulse rate 150, temperature raised. He seemed quite unconscious.

No abnormal neurologic signs were noted at this time other than a right extensor response. Earlier he had regained consciousness for a time, when the right knee jerk was said to have been weak, and a poorly sustained lateral nystagmus was present.

May 9, 1944, at 9 A.M., he was conscious, but the pulse was very rapid, and to 180 per minute. The respiratory rate had varied greatly, but at this time was from 7 to 12 a minute. The axillary temperature had varied from 103 to 104° F. His color was bluish, and respirations somewhat gasping. As his neck seemed swollen, adrenalin was given in case of glottic edema, but without effect.

The ventricles were punctured; the cerebrospinal fluid seemed under some increase in pressure and a cannula was left in the ventricle.

Death occurred on the same day.

*Autopsy.*\*—Heart, lungs, thyroid, neck, and abdominal and pelvic viscera were normal.

As the dura was incised the brain bulged through the incision. No gross abnormality was found on superficial examination, nor was anything abnormal found at the brain base, in the bones of the skull, or in the pituitary region.

Brain and pituitary gland were preserved in formalin for future examination.

*Macroscopic Examination of the Brain.*†—The surface of the brain after fixation showed no evidence of tumor, hemorrhage, or meningitis, and no cerebellar or uncus herniation. On sagittal section the following abnormalities were found:

(1) A large combined cavum septi pellucidi and cavum Vergae, its anterior extremity extending into the right frontal lobe, deformed the right anterior horn and burrowed well under the ependyma. Its lining was rough and granular. The right lateral wall was complete, but the left deficient in its posterior part.

\*Done by Dr. H. Sissons and Dr. R. Willis.

†Examination by the author.

(2) Beneath the ependyma of the lateral ventricles were numerous small cavities, with ragged walls, some communicating with the ventricle. Elsewhere the ependyma over limited areas was separated from the underlying tissue, sometimes for several millimeters (Fig. 1).

(3) A collar of grayish tissue surrounded the sylvian aqueduct, and was particularly marked on its right side (Fig. 2). In places it was from 2 to 3 mm. wide. It could be traced to within 2 to 3 mm. of the quadrigeminal plate, and forward beneath the aqueduct into the hypothalamus, particularly on the right side. It did not seem to involve, or to extend beyond, the mamillary bodies. It could be followed caudally under the ependyma into the right side of the pons, where it became more superficial under the floor of the fourth ventricle at about its middle, and where it extended at least to the lateral angle of the ventricle. It could not be observed on the left side of the pons.

(4) A grayish, slightly spongy wedge-shaped area lay in the external capsule of the left hemisphere beneath the claustrum, with its apex toward the putamen, which may have been slightly involved. In coronal section it measured 1.8 by 4 cm. Its anteroposterior measurement was not made accurately, but was considerably above 1 cm.



Fig. 1.—Coronal section of right frontal lobe, with cavum septi pellucidi on the left, showing cavities in the subependymal glia with separation of the ependyma.

*Microscopic Examination.*—Sections of the brain were stained with hematoxylin and eosin and van Gieson, and with iron hematoxylin for myelin sheaths and neuroglial fibers.

Sections were examined from representative areas of the cortex and basal ganglia, from serial coronal blocks of the hypothalamus, and from sagittal and horizontal blocks of the brain stem.

*Brain stem and hypothalamus:* Roughly corresponding to the abnormal area observed macroscopically were numerous blood vessels lying in a glial matrix (Figs. 2, 3, and 4). This glia, although often fibrillary about the vessels and beneath the ependyma, was in places highly cellular with large prominent nuclei, so that in section it was not unlike astrocytoma. Small areas containing numerous compound granular corpuscles and spaces between the glial cells, suggesting recent softening and edema, were found at the junction of aqueduct and third ventricle, and in the medulla. One small recent hemorrhage was present in the area of softening near the aqueduct (Figs. 5 and 6).

The extent of this abnormal tissue was determined as accurately as possible by numerous sections, and was as follows: The area most affected was at the junction of aqueduct and third ventricle; it did not, however, extend rostrally as far as the dorsomedian nucleus, but the substance of the posterior hypothalamic nuclei contained vascularized tissue, although the number of vessels here was not great, and both large and small nerve cells seemed normal. The mammillary bodies were entirely free of the tissue, which was limited on its inferior and lateral margins by the mammillothalamic tracts. No other nucleus of the hypothalamus showed any significant changes, although all were examined.

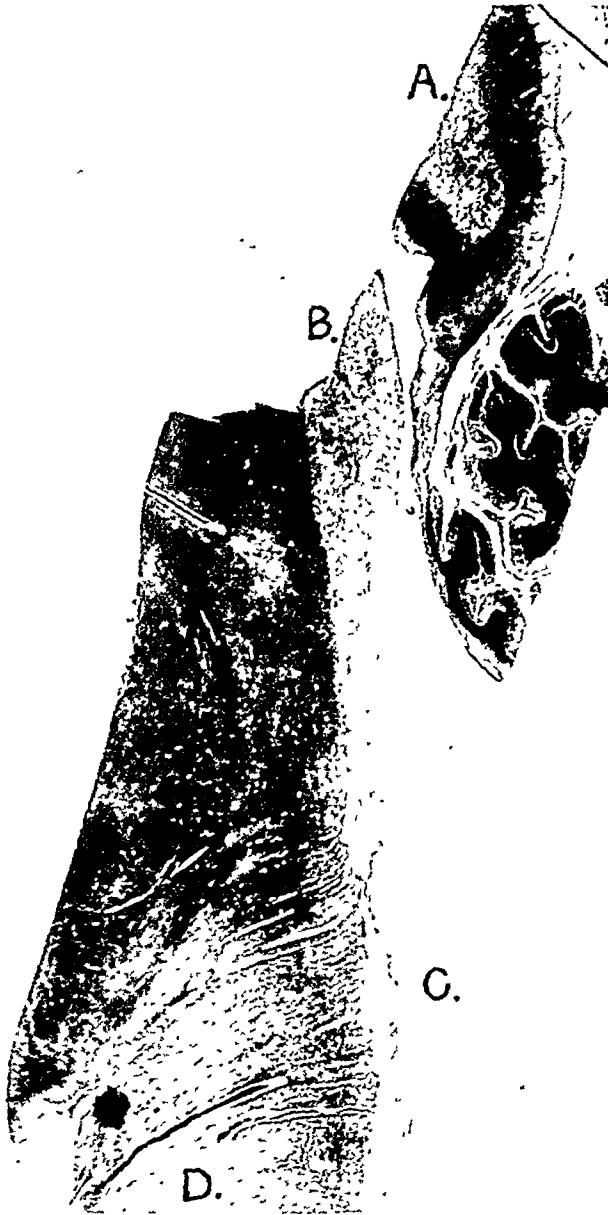


Fig. 2.—Sagittal section of lower part of the aqueduct and part of fourth ventricle. A, Vascularized and gliotic area beneath the quadrigeminal plate. B, The same anterior to the aqueduct and extending down under the floor of the ventricle C. D, The same in the pons (ironhematoxylin).

In the region of the aqueduct, especially at its rostral part, the vascularization and gliosis was most intense (Fig. 3), but the neighboring myelinated tracts and groups of nerve cells, some contained within the gliotic area, seemed healthy. On the right side, where the lesion was most extensive, numerous compound granular corpuseles were present indicating recent softening (Fig. 6). The vascularized area surrounded the aqueduct, extending caudally under the ependyma of the fourth ventricle on the right side and toward its right lateral recess.

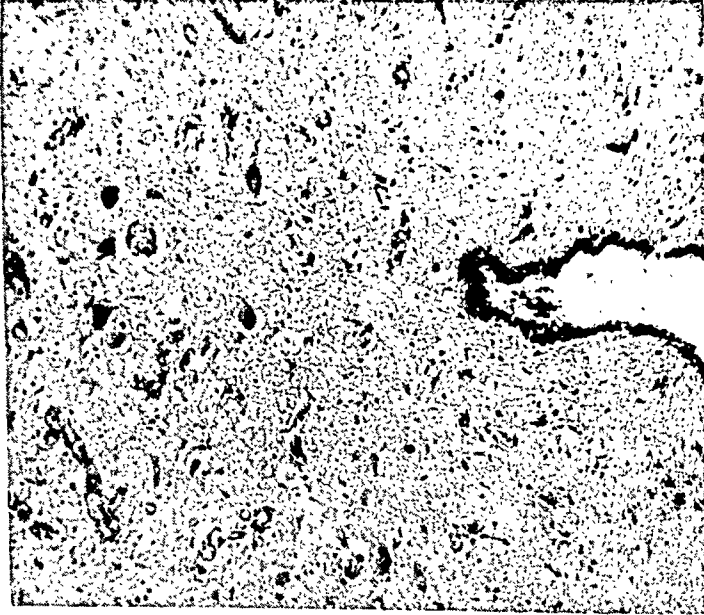


Fig. 3.—Gliotic area with new vessels near upper part of aqueduct (hematoxylin and eosin,  $\times 100$ ).

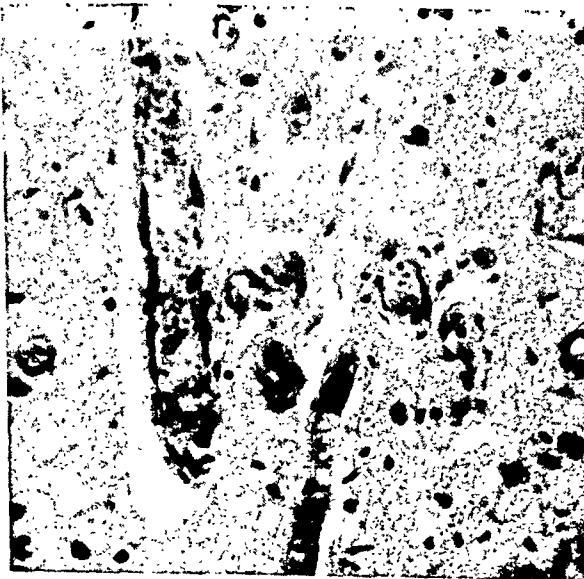


Fig. 4.—The same section as that shown in Fig. 3 revealing new vessels ( $\times 240$ ).

The left side of the floor was little involved. Below the level of the pons a large area of gliosis and vascularization was present toward the midline just posterior to the inferior olives and involving both sides. A similar area, but containing many compound granular corpuscles, and therefore probably indicating recent softening, lay inferior to it in the medulla on the right side; it was probably continuous with the higher area. At this level the ependyma at the inferior angle of the ventricle was granular and gliotic over a small area not reaching the midline, just posterior and lateral to the hypoglossal nucleus.

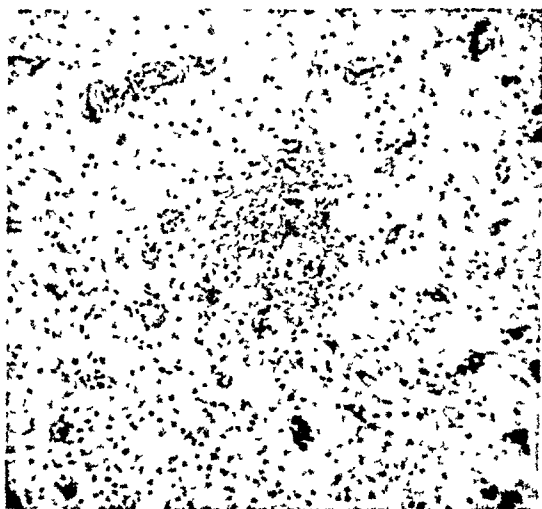


Fig. 5.—Hemorrhage in a small area of softening in the gliotic area near the upper part of the aqueduct (hematoxylin and eosin,  $\times 90$ ).

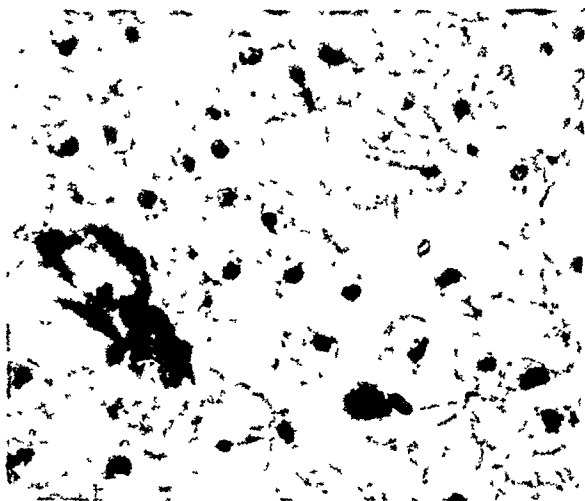


Fig. 6.—The same area of softening as that shown in Fig. 5, with compound granular corpuscles (hematoxylin and eosin,  $\times 375$ ).

The cerebral cortex appeared normal. There was, however, an increase in vessels and in neuroglial nuclei in the white matter of the hemispheres and in the basal ganglia. The abnormal area in the left external capsule proved to be a well defined area of gliosis and vascularization with strands of connective tissue (Fig. 7). There was marked gliosis about the vessels and an increase in oligodendroglia in the neighboring brain. No compound granular corpuscles were observed.

The cerebellum seemed normal and contained no new vessels or areas of gliosis.

The ependyma of the cerebral ventricles showed occasional small microscopic granules of gliosis. Almost everywhere the subependymal glia was unduly thick. The cavities noted macroscopically were entirely within the glia, rough-walled, and did not contain blood pigment. The walls of the cavum septi pellucidi and Vergae were composed of similar tissue (Fig. 8). The subependymal glia often seemed unduly vascular, and in places the glial nuclei were so



Fig. 7.—Margin of gliotic area in left external capsule (hematoxylin and eosin,  $\times 100$ ).



Fig. 8.—Section near junction of septum pellucidum and ventricular wall; septum pellucidum to the left with ragged wall of cavum (hematoxylin and eosin,  $\times 40$ ).

large and numerous that the area could readily have been mistaken for glioma. Numerous nests of ependymal cells lay within the glial zone and extended for some distance along the inferior margin of the rostrum of the corpus callosum.

The subarachnoid space contained no abnormal cells, although the arachnoid was slightly thickened, possibly from hemorrhage at the time of injury.



## DISCUSSION

*Pathologic Features.*—An opportunity to examine a brain many months after a severe head injury is not often given. In this case interest is added in that the injury was a closed one and there was no evidence at autopsy that the surface of the brain had suffered significant injury.

The following abnormal features seem worthy of record:

(1) The diffuse nature of the gliosis and vascularization, and in particular its severity at the junction of aqueduct and brain stem and about the aqueduct, and its extension under the floor of the fourth ventricle

(2) The marked participation of newly formed vessels in the reparative process along with gliosis

(3) The changes in the subependymal glial zone

(4) The presence of a few small areas containing compound granular corpuscles, suggesting recent softening

(5) The presence of a well-formed combined cavity derived from a combination of cavum septi pellucidi, and cavum Vergae

(1) The nature of the changes in the brain resulting from head injury are well known, and in particular those found in patients who died soon after trauma. Injuries of cortex and of the meninges need not here concern us, as they were not visible in this patient. There was, however, unquestionable evidence of widespread deep changes markedly involving brain stem, posterior hypothalamus, and the region adjacent to the left insula, although elsewhere present to a minor degree.

Their histologic structure was one of new vessel formation (Figs. 2 and 3) and gliosis. Such a reaction of the brain to injury is well known, new vessels being derived from those normally present, and glial cells with fibrils from the multiplication with fibril formation of classical neuroglia. Changes in vessels and neuroglia can be observed as early as the third and fourth days after injury.<sup>3, 4</sup> The reaction of all types of neuroglia to trauma has been well studied by Rand and Courville<sup>4b</sup> in early fatal cases, and the important effects of hemorrhage in producing tissue reaction have been emphasized.

However, in the late example here described there is no conclusive evidence of past hemorrhage, although it probably occurred. Gliosis and vascularization being widespread and sometimes well defined, it concerns us to know what lesions with this distribution and definition might legitimately be considered as their precursor.

Multiple hemorrhages, often of small size, have been commonly described in injury of the brain in distribution closely resembling that of the lesions under consideration, their first description in the brain and brain stem being usually attributed to Richard Bright in 1831.<sup>5</sup> Later they were reported in human beings and in traumatized animals by Duret in 1878,<sup>6</sup> and since by many others. Their common sites are the white matter of the cerebral hemispheres, brain stem, and upper cervical cord, although found in many other

positions. The gray matter of the cortex is rarely affected. It is to be observed that the zones of gliosis and vascularization in this case have appeared in those sites commonly affected by petechial hemorrhages, as for instance the region about the aqueduct, and the floor of the fourth ventricle, and the deeper part of the pons. They do not, however, always appear here experimentally, for Denny-Brown and Russell,<sup>7</sup> in extensive experiments on cats, found them most commonly in the gray matter and under the pia of the upper segments of the spinal cord.

The origin of these hemorrhages has been attributed to the force of the injury transmitted directly to the vessels, with fracture of their walls; to injury of the walls from the driving in of cerebrospinal fluid along the perivascular spaces; or to the concussive effect of injury on the vessel, with subsequent vascular dilatation, stasis of circulation, thrombosis, and anoxemia, followed by destruction of the wall. However, cases have been reported in which fresh petechiae have been observed days or weeks after injury, some of which certainly have resulted from fat embolism, but the origin of others has been uncertain and the theory of capillary stasis has again been invoked for their explanation. One small hemorrhage of recent origin in an area of softening was noted in this case (Fig. 5).

Furthermore, injury to the deeper parts of the brain, brain stem, and cord may occur without such overt evidence of injury as hemorrhage. This is clear from those cases of death attributed to concussion, where there was no visible appearance of local injury, although this must have occurred. It is also shown by areas of softening deep in the brain substance of certain acute fatal cases, and may be assumed from the widespread gliosis observed in other patients who died some time after injury. This occurrence of softening without hemorrhage is clearly seen in the patient (Case 1) reported by Winkelmann and Eckel,<sup>8</sup> who died four days after injury. The cerebellum contained many areas of softening, with early vascularization, the microphotograph somewhat resembling those of the case here reported.

From such injuries, as well as from overt bleeding, gliosis may result, changes in the neuroglia often being visible within a few days. That generalized edema is uncommon, but local edema about areas of traumatized tissue common, has been emphasized by Greenfield<sup>9</sup>; in his opinion it may cause considerable demyelination with atrophy of tissue. Areas of gliosis observed later after injury, particularly if associated with paling of the white matter as shown by myelin sheath staining, may represent areas previously affected by such edema.

Applying these observations to this case it is likely that the well-defined gliotic areas in the brain stem have resulted from small hemorrhages. Although such hemorrhages may later produce cysts, large or small, with gliotic margins,<sup>10</sup> this does not seem necessarily to follow. Many hemorrhages follow tissue planes, such as are present along vessels or between tracts of ensheathed nerve fibers; these would result in elongated areas of gliosis and vascularization without cyst formation, such as can be seen in the brain stem of this case, particularly in the subependymal zone.

The more diffuse gliosis and vascularization found in the white matter of the cerebral hemispheres could have resulted from somewhat widespread and less well-defined zones of degeneration and edema such as we have discussed. Nowhere was there clear evidence of old hemorrhage as shown by blood pigment accumulations, although occasionally microscopic cysts were observed in gliotic areas.

(2) The marked vascularization of the areas is notable. Prominent vascular endothelium has been observed even in cases of rapidly fatal head injury and evidence of new vessel formation has been observed within a few days of injury. Vascularization is a common feature in the repair of many brain lesions and may be a conspicuous feature in the reaction to many of the more malignant gliomas.

Where cortex and meninges have been injured, a highly vascularized scar can result, the composition of which has been studied by Penfield,<sup>9</sup> and Foerster and Penfield.<sup>10</sup> They have emphasized the role of this scar in the production of posttraumatic epilepsy, and that by its contraction, tension occurs between meninges and brain. The brain is thereby anchored at its area of attachment to the meninges and not permitted normal freedom of movement with respiration or with the filling of the cerebral vessels when the intracranial venous pressure is increased physiologically.

But not all patients with post-traumatic epilepsy show adhesions between cortex and meninges; at times the scar is within the brain without outward attachment yet clearly forms an epileptogenic focus in which glial and fibrous tissues are bound to new vessels. Exactly how such an area incites the epileptic attack is not clear, but it is plainly liable to changes in volume subsequent to passive engorgement for the new blood spaces usually form no muscular coat and are of the nature of capillaries. Furthermore, it is perhaps liable to certain degenerative changes; in two zones, at least, in this case there was evidence of recent lesions of a degenerative type, as shown by many compound granular corpuscles among the new vessels in the peri-aqueductal area of gliosis and in the medulla. The former lesion may have been of significance in the initiation of recent symptoms.

(3) Changes in the subependymal glia were well marked. The frequency of such changes, as well as those in the ependyma itself, can be seen in the large series of cases of fatal head injury studied by Rand and Courville.<sup>11</sup> They observed edema of the subependymal zone, sometimes with extravasation of blood and vacuolization of the ependymal cells as a common feature, shortly after injury.

It is well known that small petechial hemorrhages of traumatic origin may be situated beneath the ependyma of the ventricles, and that at times the ventricular wall may be ruptured. This might well occur in that type of injury illustrated in the experiments of Denny-Brown and Russell<sup>12</sup> and called by them "acceleration concussion." Here the suddenness of the movement subsequent to the impact of the blood could result in a dragging away of the layer lining the ventricles, from the zone to which it is attached. It may have occurred

thus in this case; in many areas the ependyma was separated from the neighboring brain tissue or contained cavities which occasionally communicated with the ventricles. Cavitation was particularly marked about the anterior horns (Fig. 1), an area which Greenfield<sup>8</sup> found susceptible to injury when the posterior part of the head receives the blow. Furthermore, in this case there were areas in which small nodes of glial cells were present, occasionally the nuclei being of large size, the histologic appearance over a small area suggesting activity and resembling a moderately cellular glioma.

(4) The presence in this case of small areas containing compound granular corpuscles and one small hemorrhage has already been noted and commented upon. It is likely that such phenomena so long after injury have resulted from changes, such as thrombosis, in newly formed vessels.

It is important to emphasize that the late effects of cerebral trauma are by no means confined to the mechanical effects of scar contraction or to adhesions restricting normal movements, but that late softening and vascular changes may occur.

(5) The large central cavity, a combination of *cavum septi pellucidi* and *cavum Vergae*, could not be claimed reasonably as the result of injury. It is not proposed, therefore, to discuss the origin and significance of this condition here; it has been well described by Dandy,<sup>11</sup> who reported two similar cysts upon which he had operated subsequent to signs of organic brain disease, their sites being correctly localized by ventriculography. He, too, has fully traversed their historical discovery and anatomic features.

It is unlikely in this case that the abnormal cavity in any way contributed to the later clinical features, for at the time of autopsy it freely communicated with the ventricles. Earlier it may not have done so. Its presence indicates an abnormality of development, possibly affecting, too, the subependymal glia in general. It is, indeed, conceivable that the subependymal glia of this patient may have been unusually well developed at birth, for everywhere it was thick and contained more ependymal rests than are commonly seen. The septum pellucidum itself represents in part the subependymal glia zone, although containing some true nervous elements. Furthermore, there were occasional small subependymal granules which were not clearly attributable to the trauma and may have been congenital. The subependymal glia of this patient, indeed, may have been more susceptible to injury than is usual.

#### CLINICAL DISCUSSION

The chief clinical interest in the patient lies in the late occurrence of somnolence, with obesity, and excessive appetite and thirst, and in an unusual epilepsy conforming in part to the periventricular or diencephalic type. All of these late phenomena can be related to the lesions of hypothalamus, periaqueductal region, and brain stem with reasonable certainty.

The day has passed when proof need be shown that lesions of the hypothalamus can produce such symptoms as undue somnolence, abnormal thirst and appetite, and obesity; this has been amply shown by observations on such conditions as neoplasms of the brain base. Experiments on animals have also

confirmed the association and have shown that injuries in particular situations may produce one or another of the abnormalities of the "hypothalamic syndrome." However, one need not attempt to overload the individual nuclei of the hypothalamus with such restricted functions as the control of sleep, the vasomotor system, or body temperature, even if there is much evidence to show that certain nuclei may modify individual functions, mainly through their connections with hypophysis, for the supraoptic nucleus by its control of the anti-diuretic hormone is related to water metabolism, its injury resulting in diabetes insipidus, and the ventromedial nucleus may control the diabetogenic hormone with the production of diabetes mellitus at its injury. Such a clear allocation of function has not been shown for the posterior nuclei, even though it may be generally stated that the posterior hypothalamic area plays some role in the coordination of some sympathetic reflexes, and the anterior a smaller part in coordination of parasympathetic reflexes.<sup>12a</sup>

The physiologic functions which were altered in this patient were those of sleep, appetite, thirst, and control of heart and respiration. Furthermore, the gain of weight suggested a metabolic change.

Excessive sleep has been frequently produced by lesions of the hypothalamus, through disease, or by animal experimentation. In animals, Beattie, Brow, and Long<sup>13</sup> found its production outstanding in those which survived section of the tracts between the anterior edge of the superior colliculus and the mammillary bodies. These results have been confirmed by experiments with the stereotaxic instrument in which it has been possible to destroy the gray matter surrounding the opening of the aqueduct into the third ventricle, with only a small amount of surrounding tissue.<sup>12a</sup> Ingram, Barris, and Ranson<sup>14</sup> found somnolence to be best produced by lesions between the mammillary bodies and the third nerve nucleus. As in both groups of experiments there need be no injury of the long motor or sensory tracts, they agree that destruction of the efferent hypothalamic connections is the essential feature.

How these lesions cause somnolence is as yet unproved. To some the sleep impulse is an active inborn process analogous to an instinct; it is something so vital to the organism and appearing in so many species, that it seems a mechanism must exist for its promotion. I have allied myself to this view<sup>15</sup> and am of the opinion that it may yet be shown that pathologic somnolence of the type being considered results from the physiologic release of an inborn mechanism, which thereby overacts. Others regard it likely that a mechanism for attention exists and that the lesions of the hypothalamus or thalamus prevent it exerting its control, body and brain thereby falling into a resting state through lack of rousing.

Whatever the correct explanation, it is certain that other changes in consciousness, such as catatonia, and trancelike states similar to, but not identical with, sleep may be encountered with pathologic lesions in this neighborhood. I have reviewed the subject with illustrative cases,<sup>15</sup> and more recently it has been reviewed by Alpers.<sup>16a</sup> That the loss of consciousness in concussion may be derived from a disturbance in such a mechanism is no new view; the idea

that concussion is produced through lesions of the brain stem is many years old, and recently the resemblance of the loss of consciousness to sleep has engaged the attention of Eden and Turner<sup>17</sup> and Jefferson.<sup>18</sup>

Furthermore, sleep is intimately bound up with physiologic effects of the vegetative type; it is not surprising, therefore, to find disorders of these functions with lesions of the hypothalamus which produce hypersomnia.

Obesity is also a common association of hypothalamic lesions, although as yet there is no certainty as to its mode of origin. It may occur with lesions of the hypophysis as well as of the hypothalamus. Excessive appetite and thirst are often its associates, and all, although not of necessity, are associated with hypersomnia. Large lesions of the tuberal region seem most likely to produce obesity experimentally.

It is of interest to note that in this case with all these symptoms present, the mammillary bodies were not involved, and of the hypothalamic nuclei, only the posterior group was involved, although both large and small nerve cells seemed normal histologically. However, as these cells lie in the course of the periventricular system of fibers and seem to be an important source of its origin, it is likely that involvement of the tract, rather than any particular group of nerve cells, as in animal experiments, is the essential lesion in hypersomnia. Indeed, it can be seen in this case that the zone of vascularization and gliosis in hypothalamus, mesencephalon, and pons closely followed the course of these fibers. The periventricular system is considered an efferent pathway from the hypothalamus carrying impulses from diverse hypothalamic nuclei to the brain stem and perhaps to the spinal cord.<sup>12b, 16b</sup> As the fibers are related to nuclei of the motor cranial nerves and of the reticular substance, it is likely that they are concerned with visceromotor functions. Therefore, it is not difficult to imagine that such functions could be disturbed with lesions of the hypothalamus and brain stem of the type discovered in this patient.

The reason for the late incidence of the hypothalamic symptoms is by no means clear. Why should such phenomena occur late, rather than early, when the lesions were presumably at their maximum? Is there evidence for progression in traumatic lesions of the cerebrum?

There is no easy explanation for these late phenomena. Should they require a paralytic lesion for their production, such was certainly present in the early stage of injury. It has already been noted that there was evidence in this patient of a recent lesion at the junction of aqueduct and third ventricle, as well as in the medulla; in the former lesion numerous compound granular corpuscles, one small recent hemorrhage, and some separation of glia cells suggesting edema were present on the right side.

If, however, in analogy with ordinary post-traumatic epilepsy, a focus of irritation is thought to be the initiator of the epilepsy, we can regard this same area of softening as an adequate cause or fall back on that explanation usually deemed sufficient for this condition, irritation from the contraction of connective tissue and glia in the process of repair, with alterations in volume of the new vascular bed. Either view might imply that the hypothalamic syndrome of

obesity, excessive appetite, and thirst with hypersomnia also arose from a constant or frequent irritative process, and the later epileptic condition with the respiratory and cardiovascular disturbance, raised temperature, disturbance of consciousness with excessive hunger was but the result of a greater and more widely spreading discharge.

Attacks of this type were described by Gowers<sup>19</sup> as vasovagal attacks, and by Wilson<sup>1</sup> as periventricular epilepsy. There was little satisfactory pathologic confirmation for these early cases, but Penfield's patient<sup>2</sup> who suffered attacks of restlessness, with thirst, a sensation of heat, vasomotor changes, sweating, laceration and salivation, pupillary changes, and sometimes exophthalmos, was found to have a tumor involving both foramina of Monro. McLean's case<sup>20</sup> was also of this type. With the attacks were emotional changes, dyspnea, oppression of the chest, tachycardia, hunger, and impulsive weeping; a large basal tumor was present. One of my patients (Case 6<sup>15</sup>) suffered from turns of mental distress with respiratory and vasomotor changes. He was found to have a pituitary tumor and was relieved by operation.

Nevertheless, small circumscribed lesions have not usually been found at autopsy. Even in the patient here described other lesions than those in the hypothalamus and brain stem were present; thus, besides widespread changes in the white matter and the basal ganglia, a large lesion was found in the left claustrum. That a hypothalamic lesion was present was thought possible, clinically, from earlier experience with basal tumors, and it seems highly probable that the lesion in brain stem and hypothalamus was the exciting cause of the late symptoms.

The hemiplegia early in the illness is presumed to have resulted from the large lesion in the left insular area.

#### SUMMARY

1. A boy, aged 8 years, although apparently recovering well from a severe head injury, developed, after thirteen months, voracious appetite, thirst, rapid gain of weight, and undue sleepiness.

2. One month later he developed attacks, with vasomotor and respiratory changes, and hunger, in which he usually became sleepy or semiconscious. Sometimes clonic contractions of the limbs were present. During their course he died.

3. At autopsy a prominent area of gliosis and new vessel formation surrounded the aqueduct, extending well down into the brain stem. Lesser changes were present elsewhere, although a gliotic area was present in the left internal capsule. There were a few areas of recent softening.

4. The hypothalamic nuclei were not affected, the lesion appearing chiefly to affect the zone of the periventricular fibers.

5. There was considerable cavity formation in the subependymal glia of the ventricles, and a large combined cavum septi pellucidi and cavum Vergae was present.

6. The relation of the pathologic condition to the injury and its anatomic and clinical implications are briefly discussed.

I am indebted to Dr. H. C. Trumble, with whom I saw this patient, for permission to study and describe the brain; and to Professor R. Willis and to Dr. H. Sissons for the photographs.

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# CONTRALATERAL, IPSILATERAL, AND BILATERAL REPRESENTATION OF CUTANEOUS RECEPTORS IN SOMATIC AREAS I AND II OF THE CEREBRAL CORTEX OF PIG, SHEEP, AND OTHER MAMMALS

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## INTRODUCTION

**S**TUDY of central afferent systems by recording electrical potential changes evoked on physiologic stimulation of peripheral receptors or by electrical excitation of peripheral nerve fibers, as distinct from observation of spontaneous electrical rhythms or of potential changes induced by local applications of strychnine,<sup>23</sup> is now a well-established anatomicophysiologic procedure. It has been successfully employed on the cerebral cortex for investigating localization in the somatic,<sup>1, 2, 4, 10, 11, 28-30, 37, 38, 54, 55, 57, 58, 60</sup> the visual,<sup>29, 35, 36, 39, 45-48</sup> the olfactory,<sup>3, 8, 26, 43</sup> and the auditory systems.<sup>6, 7, 14, 15, 34, 49, 52, 59</sup> In the cerebellum it has revealed that not only vestibular<sup>21</sup> and proprioceptive impulses<sup>22</sup> but also visual,<sup>44</sup> auditory,<sup>44</sup> and tactile<sup>5, 22, 44</sup> messages are received by this organ in well-organized systematic fashion.

With animals under satisfactory barbiturate anesthesia, careful research reveals in great detail the manner in which the various receptor surfaces are represented in the central structures and makes possible comparative functional and morphologic investigations unattainable with any other method. It is becoming evident that the evoked potential technique permits identification of certain homologous cortical areas more definitely than does the cytoarchitectonic method and in addition it makes possible detailed comparison of relationships within homologous areas. Clearly, combination of electrical technique with classical anatomic and physiologic procedures will result in great refinement of our knowledge of functional organization within the nervous system.

The time is now at hand for the study of cortical potentials evoked in man at neurosurgical operations. It is particularly important, therefore, in order that significant answers be secured that general principles of cortical organization be defined clearly by comparative studies on lower forms.

Until now it has been customary to think of each of the main afferent systems as having a single primary pathway into the cerebral cortex. The present study and earlier observations on cat,<sup>1, 54</sup> dog,<sup>54</sup> monkey,<sup>54, 55</sup> and rabbit<sup>60</sup> show that the somatic system has two distinct afferent areas with separate pathways.<sup>60</sup> The same has been found also for the visual<sup>45, 48</sup> and the auditory<sup>49, 59</sup> systems. Duality, therefore, appears to be a general principle of cortical organization.\*

\*In discussing these dual systems we shall refer to them as somatic areas I and II, visual areas I and II, and auditory areas I and II. This terminology was chosen because it carries no anatomic or functional implications and because it can be applied to each of the three systems. Moreover, area I corresponds to what has been considered until now the primary receptive area of each system. Area II in each case was "second" with respect to area I in time of discovery.

In the present study we have undertaken to answer certain questions raised by the recent observations of Adrian<sup>4</sup> on the ungulate brain. Previous studies on monkey,<sup>55, 57</sup> cat,<sup>30, 54</sup> dog,<sup>54</sup> and rabbit<sup>60</sup> had led us to the generalization that in each of these species the somatic receiving areas are fundamentally similar. Homologous subdivisions of the "postcentral" area (somatic area I) are identifiable in each animal. The area differs from species to species, not basically but, in the relative development of its various subdivisions, apparently in accord with the specialization of the corresponding peripheral receptor surfaces in individual species. In somatic area I all responses had been found to be strictly contralateral, with the exception of a part of the face area of the monkey.<sup>57</sup> Besides the "postcentral" area we have found in each species an area (somatic area II) homologous with Adrian's<sup>1, 2</sup> "second" somatic receiving area of the cat. In rabbit, cat, and dog this area is situated lateral to somatic area I and anterior to the auditory areas (Fig. 6, A and B); in monkey it lies chiefly on the dorsal wall of the sylvian fissure in similar relationship to somatic area I of the postcentral gyrus and to the auditory areas (Fig. 6, C). Our studies have shown that in somatic area II both halves of the cutaneous surface are represented in each cerebral cortex. Contralateral responses are approximately twice as large as corresponding ipsilateral ones. The apical portions of the body (digits, snout, and tail) give largest responses on stimulation, and under deep anesthesia the apices of the contralateral half of the body alone may activate the cortex. There is spatial differentiation within somatic area II and this increases from rabbit to monkey but it is much less than the increasing differentiation within somatic area I. It does not reflect the specialization of receptor surfaces as does somatic I.

Adrian's<sup>4</sup> study on ungulates indicated that from the face only receptors in lips and snout sent impulses to the cortex. In sheep and goat these impulses were ipsilateral while in pig and horse they were contralateral. In addition, responses to stimulation of the contralateral forelimb and sometimes of the contralateral hindlimb were observed in the anterior ectosylvian gyrus of goat, sheep, and horse. No responses from the limbs were evoked in pig and in none of the species was any response to limb stimulation detected in areas possibly homologous with postcentral gyrus.

To relate these findings on ungulates to results on other species, observations were made on one sheep and seven pigs (the numbers being dictated by supply). We soon found in sheep and in pig both the contralateral face area of pig and horse and the ipsilateral face area of sheep and goat. Most of the previously defined characteristics of somatic area II were established also for sheep and pig, and in addition the arm subdivision of somatic area I was located in pig. (It was not looked for in sheep.) A hindlimb subdivision of somatic I was not found but its probable locus was suggested.

With discovery of the ipsilateral face area in pig and with the existing evidence for a bilateral face area in monkey, search was made for a homologous area in cat and dog. This was found in both species, thereby establishing for all animals studied a basic plan of cortical organization. Data from the literature will be cited with a view to relating some of the findings to man.

## MATERIALS AND METHODS

The animals used in this study consisted of three Yorkshire and four Hampshire pigs, aged 5 to 8 months, one sheep, aged 4 months, two cats and one dog.

All animals were anesthetized with pentobarbital sodium, administered intraperitoneally, except for four of the pigs, which were given a combination of pentobarbital and chloralose. Initial dosage of pentobarbital was 42 mg. per kilogram. Anesthesia was maintained as evenly as possible by periodic injections of additional amounts (every twenty minutes in case of pig). In the pigs the maintenance dose of pentobarbital was found to increase with weight from 5.5 mg. per kilogram per hour for a pig weighing 9.5 kilograms to 15.0 mg. per kilogram per hour for one weighing 17.4 kilograms. Chloralose in the amounts used (11 to 33 mg. per kilogram per hour, approximately) had little if any anesthetic effect; the maintenance dose of pentobarbital was the same for animals of equal size whether or not chloralose was given.

Chloralose was employed to facilitate transmission of afferent impulses to the cortex. This seemed clearly to be its effect because cortical responses were more easily evoked in the animals to which this drug was given and it was only in these animals that light tactile stimuli were adequate. Pigs under pentobarbital-chloralose anesthesia reacted more like cats under pentobarbital alone and did not show the convulsive features exhibited by cats under chloralose.

The pigs and the sheep salivated profusely. To avoid difficulty with respiration it was necessary to cannulate the trachea and to ligate the trachea above the cannula.

In exposing the brain the soft tissues were removed from the skull with a Davis-Bovie electrosurgical unit. The skull was then trephined and the bone removed with rongeurs over the entire dorsolateral surface of one hemisphere. In three of the pigs both hemispheres were exposed in the course of the experiment. In certain instances cortex on one wall of a fissure was examined after the cortex of the opposing wall was carefully removed by suction.

Before exposure of the brain the head was immobilized in a holding apparatus. Later a movable electrode carrier was attached to the headholder in such a way that the exploring electrode (made of steel tubing and a core of No. 50 cotton thread moistened with saline solution) could be moved over the cortex in millimeter steps along rectangular coordinates. The "indifferent" electrode was clipped to the scalp, usually in the frontal region. To prevent drying, the exposed cortex was covered with mineral oil.

The methods of stimulation and the apparatus for amplifying and recording the cortical electrical responses have been described elsewhere.<sup>37, 38, 57, 59</sup> The cutaneous stimulator consisted of a lever rigidly attached to the moving armature of an electromagnetic device whose coils were energized by a pulse 3 to 5 milliseconds in duration. A regular, quick, to-and-fro movement resulted, which produced at the end of the lever a small displacement lasting a few milliseconds. For tactile stimulation a camel's-hair brush was attached to the lever's end. For stronger stimulation the lever itself was used or a wire was mounted at right angles to the end of the bar. The action of the stimulator was synchronized with the sweep of the cathode ray tube, thus making it possible to visualize and to photograph the response produced by each stimulation.

## RESULTS

Fig. 1 is a composite diagram illustrating the results obtained in the seven pigs. The brain is not oriented in the conventional manner, but is inverted, as are the other brain drawings in this paper. This arrangement was chosen in order to place the head uppermost in the figures and to put the feet down. We believe this aids in visualizing the plan of cortical organization, especially with respect to details within the face area (see Fig. 5), since the parts represented fall into position in the diagram in essentially the same relationships as exist in the actual face. The figure shows (1) the auditory area (*AUD.*), (2) somatic area II with its face (*F<sub>II</sub>*), arm (*A<sub>II</sub>*) and leg (*L<sub>II</sub>*) subdivisions, (3) the face (*F<sub>I</sub>*) subdivision of somatic area I (that is, the contralateral snout area of Adrian),<sup>4</sup> (4) the ipsilateral face area (*IPSI.*), which is homologous with Adrian's ipsilateral face area for sheep and goat, (5) the arm subdivision (*A<sub>I</sub>*) of somatic area I and (6) the probable location of the leg subdivision (*L<sub>I</sub>*) of somatic I on the mesial aspect of the hemisphere.

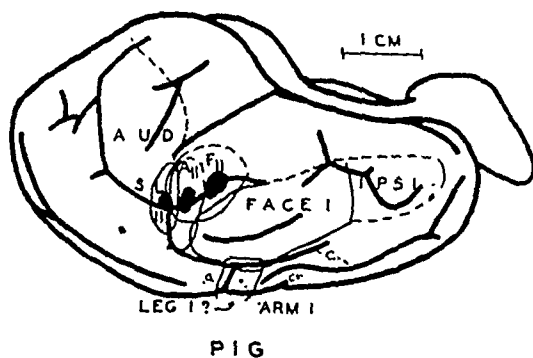


FIG. 1.—Composite diagram summarizing results obtained on seven pigs. The thin continuous lines mark boundaries determined by the experiments; the broken lines are provisional. The solid black areas represent foci of largest response to stimulation of face (*F<sub>II</sub>*), arm (*A<sub>II</sub>*) and leg (*L<sub>II</sub>*) subdivisions of somatic II. For further description see text. Labeled fissures in Figs. 1 and 2 are: a., ansate; c., coronal; cr., cruciate; s., suprasylvian.

Data for Fig. 1 were obtained on examination of ten hemispheres in seven pigs. Not all the areas illustrated were examined in each hemisphere. Observations were made on somatic area II in nine, on contralateral face area of somatic I in nine, on ipsilateral face area in four, and on the arm area of somatic I in nine. A hindlimb subdivision of somatic I was searched for on the dorsal surface of the hemisphere in most of the animals but it was not found there. The supply of animals gave out before a satisfactory examination of the mesial surface could be made, but since arm area I extends to the midline, it is likely that leg area I is to be found on the mesial aspect of the hemisphere.

Fig. 2 illustrates our findings on the one sheep studied. In this experiment it was possible to locate (1) the auditory area (*AUD.*), (2) somatic area II with face (*F<sub>II</sub>*), arm (*A<sub>II</sub>*) and leg (*L<sub>II</sub>*) subdivisions, (3) Adrian's ipsilateral face area (*IPSI.*) and (4) a contralateral face area (*F<sub>I</sub>*) homologous with the contralateral face area of the pig. Arm and leg subdivisions of somatic I were not looked for.

Pigs and sheep proved much more difficult animals in which to study evoked potentials than have other animals with which we have had experience. The barbiturates, which have been the anesthetic of choice for evoked potential studies, were found to depress transmission in the afferent systems of these ungulates before they quieted the animals generally or suppressed the spontaneous brain wave activity. With prolongation of the anesthesia, however, transmission improved and reliable results were secured, but the difficulties necessarily limited the amount of information which could be obtained from each animal. In the later experiments pentobarbital-chloralose anesthesia was found to give a preparation more like cat under pentobarbital alone and from these animals more data were collected. In spite of these limitations the results obtained showed excellent agreement when data from all animals were assembled. We are confident, therefore, that the positive findings will stand. Our data are also in excellent agreement with the positive findings reported by Adrian.<sup>4</sup>

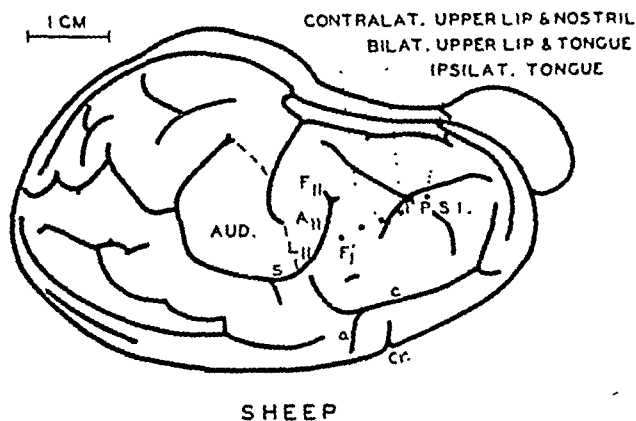


Fig. 2.—For description see text.

Fig. 3 shows the character of the electrical potential changes produced in the cortex of the pig by localized mechanical stimulation of cutaneous receptors. Responses *A* and *B* were recorded from a point in the arm subdivision of somatic area I (point *A* in Fig. 5, C). Response *A* was evoked by stimulating with a camel's-hair brush the skin over the anterior aspect of the contralateral forelimb just above the interdigital web. Response *B* resulted from stimulation of the same spot with a wire mounted on the lever arm of the stimulator. Both responses are initially surface positive but the time to maximum is shorter in *B*. Records *E*, *F*, and *G* were obtained in another animal from a point in the arm subdivision of somatic area II (point *E*, Fig. 4, B). *E* was produced by stimulating the skin above the interdigital web of the contralateral forelimb and a camel's-hair brush. *F* resulted from stimulation of the same cutaneous spot with the wire and *G* was evoked by wire stimulation of the corresponding point on the ipsilateral forelimb. It can be seen that the latencies, the times to maximum, and the durations of the surface positive waves of the somatic I responses are shorter than those of the somatic II responses. The differences in

form are due, in part at least, to differences in the time constants of the interstage couplings of the amplifier (see *D* and *I*). The longer times to maximum of responses *A* and *E* may be attributable to the less abrupt onset of stimulation by the brush as compared with the wire. Of the somatic II responses the ipsilateral has a longer latency than the contralateral. Usually the ipsilateral response was not more than one-half as large as the contralateral. In the records shown they are nearly equal in amplitude. Some observed values for the times to maximum were as follows: auditory responses, 22 milliseconds; contralateral face II, 22 to 32 milliseconds; contralateral arm II, 25 to 36 milliseconds; contralateral leg II, 45 to 48 milliseconds; contralateral and ipsilateral face I, 15 to 24 milliseconds; arm I, 20 to 22 milliseconds.

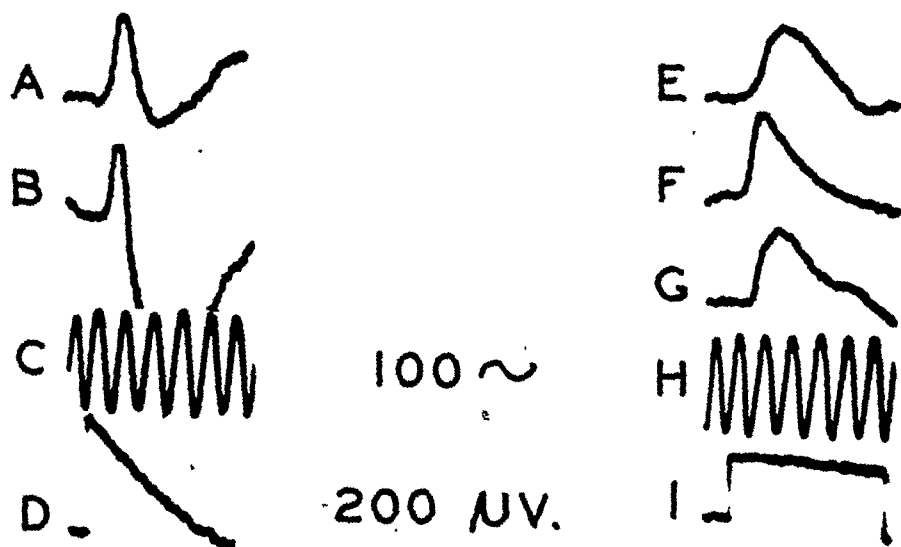


Fig. 3.—Surface positive cortical potentials evoked by stimulation of cutaneous receptors in the forefoot. See text. Records *C* and *H* are time signals and *D* and *I* are calibration potentials.

In working out relations of cortex to cutaneous surface, two types of experimental procedure may be employed. In one method a fixed point on the cutaneous surface is stimulated mechanically at approximately one-second intervals and the cortex is examined by moving the exploring electrode in 2 mm. steps along rectangular coordinates. In this way the cortical areas of response corresponding to particular cutaneous spots stimulated may be defined (Marshall, Woolsey, and Bard,<sup>38</sup> 1941). In the second method the cortex is examined point by point and for each cortical point studied the entire body surface is explored with the tactile stimulator to determine whether or not any peripheral area sends impulses to that cortical point. When a cutaneous area related to a cortical point is located, its borders are carefully delimited and the amplitudes of cortical potentials evoked by stimulation of various portions of the area are noted. This procedure defines the cutaneous areas related to corresponding cortical points and locates the peripheral locus giving largest responses at each cortical point (Woolsey, Marshall, and Bard,<sup>37</sup> 1942). The two methods reveal different aspects of cortical organization and with sufficient

observations the results of either procedure may be derived from data obtained with the other.

Fig. 4, A shows the responses evoked in somatic area I (Fig. 4, B) by light pressure stimulation of a fixed point on the dorsum of the contralateral forelimb. The cortical area defined is fairly extensive but it must also extend into the adjacent fissures. The largest responses of shortest latency, however, are fairly well localized. If one delimits the cortical response areas for a number of spatially separated cutaneous spots on the contralateral forelimb, the cortical areas are found to overlap one another greatly but the locus of the maximal

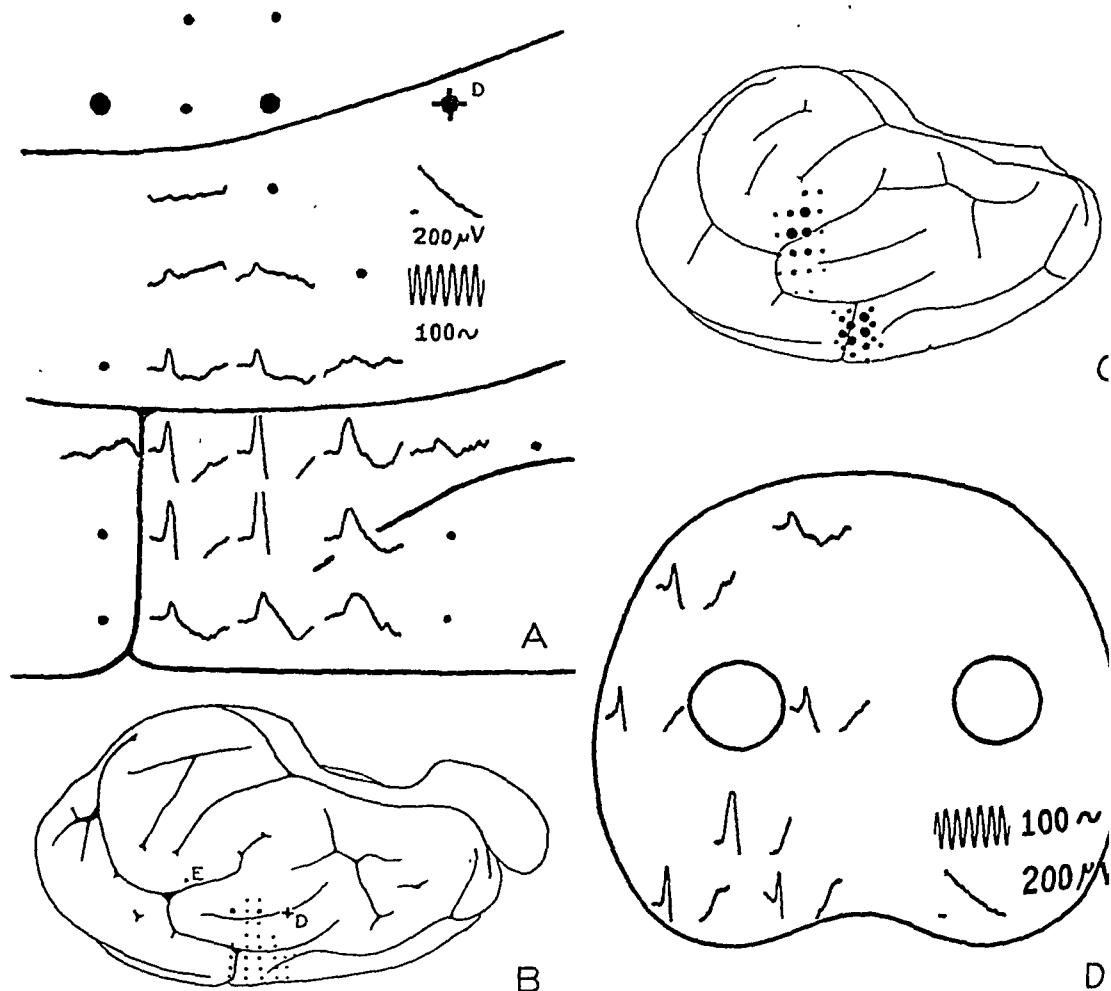


Fig. 4.—A, Cortical potentials evoked in arm subdivision of somatic area I by light tactile stimulation of the skin of the contralateral forefoot just above the interdigital web, volar aspect. Dots indicate points which yielded no response.

B, Drawing, after a photograph, of the brain from which potentials in A were recorded. The small dots represent cortical points examined and correspond to dots and records in A. The large dots are points in the face area for which skin areas activating the points were defined (see Fig. 5). From point D the responses shown in D were recorded. The dots in B are 2 mm. apart along rectangular coordinate.

C, Fields of response in somatic areas I and II to stimulation of contralateral forefoot. The diameter of each dot is proportional to the amplitude of the response at the point.

D, Responses evoked at point D in B on stimulation of various spots on the snout with a camel's-hair brush.

response is at a slightly different point on the cortex for each cutaneous spot. This arrangement no doubt provides not only a basis for local sign but also a mechanism for cortical integrations.

In Fig. 4, C the cortical areas of response to stimulation of a spot on the dorsum of the contralateral forelimb just above the interdigital web are indicated by dots whose diameters are proportional to the amplitudes of the responses observed at the corresponding points. There are two response areas. One is in somatic area I and the other is in somatic area II. In this experiment the response area in somatic I was found to extend into the ansate sulcus posterior to it and the response area in somatic II was followed to the bottom of the suprasylvian sulcus which cuts through the area. It should be noted that in addition to these two areas in the contralateral hemisphere, responses to the same stimulations must also have occurred in somatic area II of the ipsilateral hemisphere.

Data obtained with the second method are shown in Fig. 4, D. The exploring electrode was placed on a point in the contralateral face area (point D in Fig. 4, B). The cutaneous area activating the point was then found to be the contralateral half of the snout. Light tactile stimulation alone was adequate and with this no responses were evoked on ipsilateral stimulation. Largest responses with shortest latencies were obtained on stimulating the snout below the nostril. The records shown in Fig. 4, D represent the responses evoked at the cortical point when the part of the snout on which the record is mounted was stimulated. For systematic mapping of the cortex this second method produces more useful data in a given period of time than does the first method. Data of the type shown in Fig. 4, D may be transformed into small figures for assembling into charts by representing in black the cutaneous area producing largest responses and by lining the surrounding portions which yield smaller responses. In this way the figurines composing Fig. 5 were constructed. Each figurine was then mounted on a diagram of the brain in a position corresponding to the point on the cortex to which the cutaneous area illustrated sent impulses.

Fig. 5 is a composite chart made from data collected in four experiments. The figurines from each experiment were fitted together by superimposing drawings of the individual brains and matching the corresponding fissures as closely as possible. Fig. 5, C, which is also a composite drawing, shows the relations of the charted areas to the gross morphology of the brain. It must be emphasized that the results shown represent an incomplete map of the receiving areas of the pig. This is evident if one compares the data for arm subdivision of somatic area I, as shown in Fig. 4, A and in Fig. 5. But other portions of the map are also deficient, for example, the ventrolateral portion of somatic area II and parts of the contralateral and ipsilateral face subdivisions of somatic I. Large portions of the receiving areas must also exist in the various fissures. These have been explored only in part. It can be seen from Fig. 5 that the contralateral face area includes the medial bank of the coronal sulcus. It, therefore, must also occupy the lateral bank of the sulcus. The suprasylvian sulcus is nearly 1 cm. deep. Somatic area II descends to the bottom of this sulcus on its lateral bank, as we know from direct examination, but the results shown in Fig. 4, C indicate that it must cover the medial bank as well. In two of the



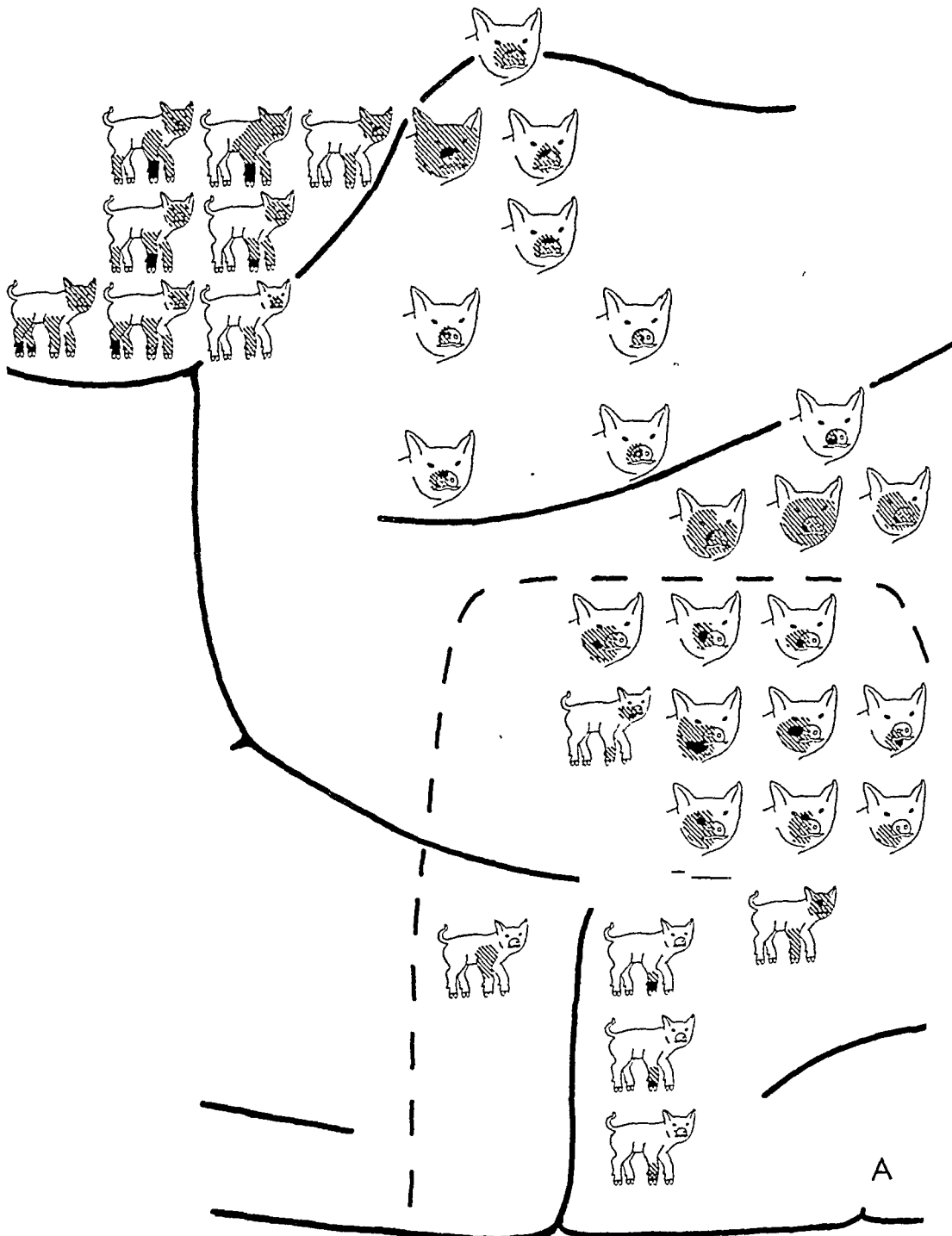


Fig. 5.—Each figurine in this chart shows the cutaneous area which sent impulses to the cortical point on which the figurine is centered. Largest responses were evoked by stimulating the area outlined in solid black. The two parts of the figure, A and B, correspond to the regions outlined by the dotted lines in C. The broken line in A delimits cortex on the medial bank of the coronal sulcus and the anterior bank of the ansate, exposed by removing opposing banks. Points on these banks are indicated by elongated dots.

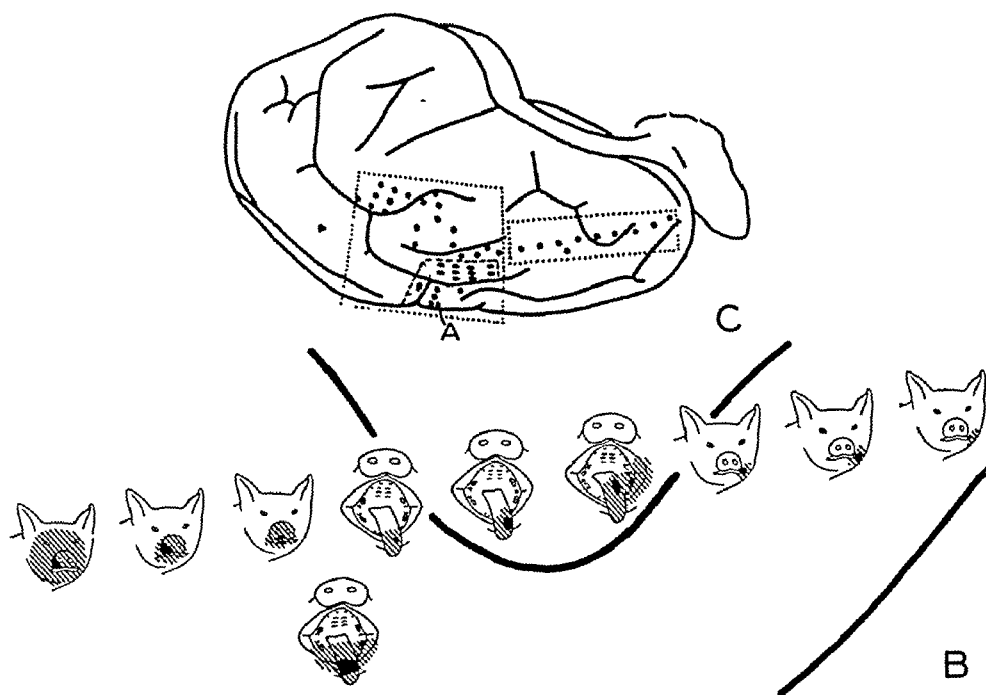


Fig. 5.—Cont'd.

pigs studied the hindlimb portion of somatic area II was entirely within the suprasylvian sulcus and in one it extended medial to the suprasylvian, posterior to the coronal (see Fig. 1).

Attention is called to several features of Fig. 5: (1) The relations of the cutaneous surface to the cortex are bilateral in somatic area II. This is quite clear with respect to the limbs where the possibility of mechanical transmission of the stimulus from one side to the other was eliminated. Controls to minimize this factor in the snout indicated that here too the bilateral relations were real. As the shading in the figures indicates, the contralateral responses characteristically were larger than the ipsilateral responses. (2) There is considerable overlapping of somatic II face, arm, and leg subdivisions, but the maximal response at each point is from either face, arm, or leg. (3) Somatic area II receives impulses principally from the apices of the limbs and from the upper part of the snout. Few responses were evoked by stimulation of the trunk, but in some pigs large potentials were observed on stimulation of the tail. (4) At several points within the contralateral face area the figurines show that the peripheral areas for these points extend to both sides of the body. Bilaterality here may be artefactual because of the strong stimuli employed. In any case, the responses were much larger contralaterally for all points in this portion of the face area. Moreover, no ipsilateral effects were ever produced in this area by brush stimulation alone. (5) Within the contralateral face area the pattern of representation on the free surface of the cortex is the same as that described by Adrian.<sup>4</sup> The lower part of the snout is represented rostrally in the area, the

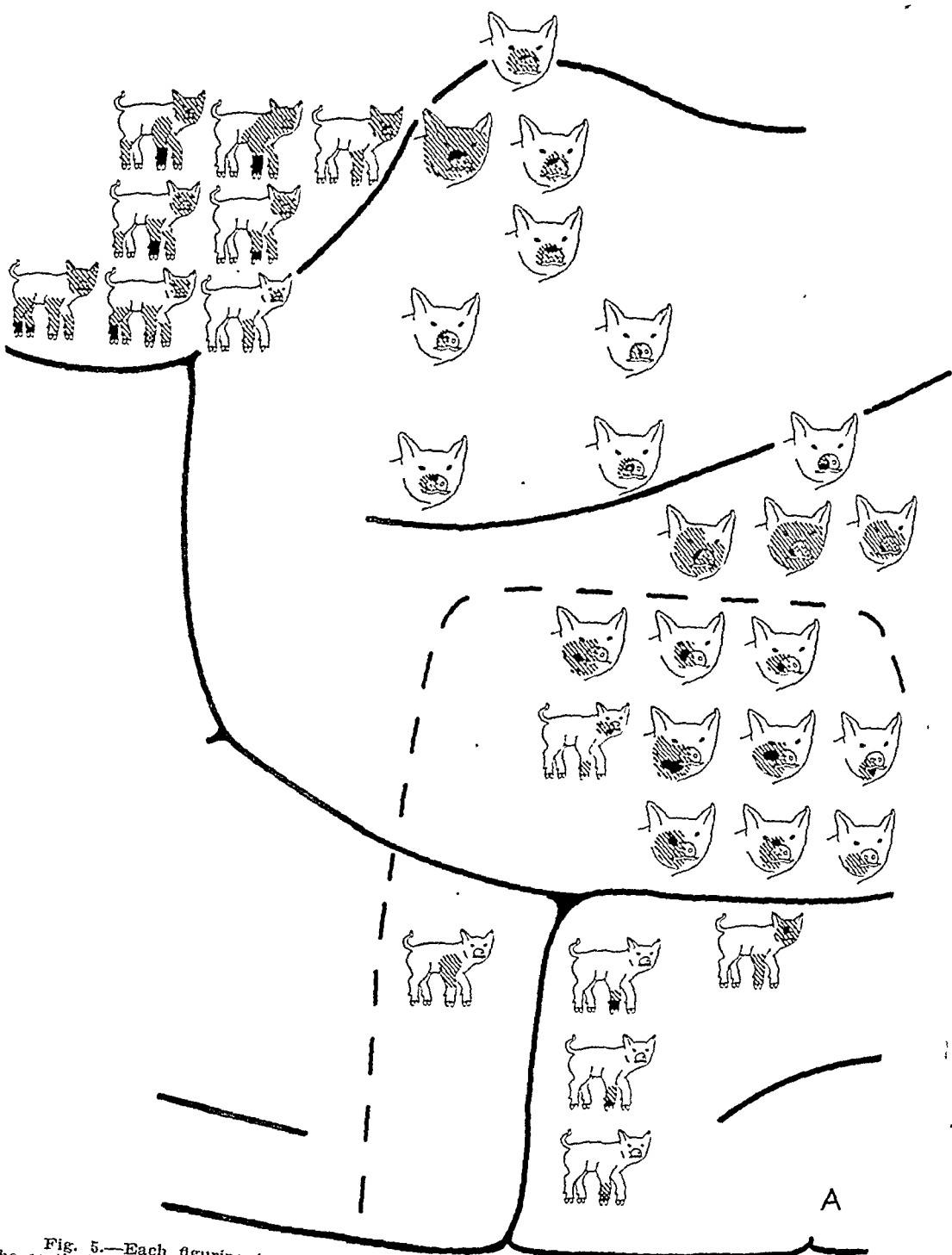


Fig. 5.—Each figurine in this chart shows the cortical point on which the figurine is centered. Largest responses were evoked by stimulating the area outlined in solid black. The two parts of the figure, A and B, correspond to the regions outlined by the dotted lines in C. The broken line in A delimits cortex on the medial bank of the coronal sulcus and the anterior bank of the ansate, exposed by removing opposing banks. Points on these banks are indicated by elongated dots.

Somatic I arm area gave responses chiefly on stimulation of the distal segments of the limb. One point for the shoulder was found within the ansate sulcus.

When it was found that ipsilateral and contralateral face areas were present both in pig and in sheep, search was made for a homologous area in cat and in dog. It was located in both species rather well forward in the hemisphere, rostral to the contralateral face area. The area in these animals, although of much smaller dimensions, showed the same general relationships as in the ungulates (Fig. 6, B).

#### DISCUSSION

The electrical technique of recording potential changes evoked by cutaneous stimulation now has been applied in this laboratory to the study of localization in somatic afferent areas of the cerebral cortex in monkey,<sup>37, 38, 54, 55, 57</sup> cat,<sup>30, 38, 54</sup> dog,<sup>54</sup> rabbit,<sup>60</sup> sheep, and pig. From these and from papers by Adrian<sup>1, 2, 4</sup> as well as from studies on auditory<sup>49, 59</sup> and visual<sup>45, 46, 48</sup> systems certain generalizations concerning cortical organization are possible. We shall summarize the story as it has developed and emphasize the basic principles which have been revealed. The results, we believe, have important bearings on the problem of cerebral localization in man, especially since it is now feasible to extend this type of study to man himself.

In 1937 Marshall, Woolsey, and Bard<sup>10, 11, 37, 57</sup> made use of the method of "evoked cortical potentials" (as distinct from spontaneous brain rhythms and potential changes induced by local applications of strychnine) to obtain a map of the somesthetic area of the postcentral gyrus of the monkey. They employed discrete light tactile stimuli, "usually mechanical displacement of a few hairs on the body surface, and observed on the synchronized sweep of a cathode ray tube the amplified electrical potential changes produced in the cortex. For each cortical point examined in the total area, they defined the extent of cutaneous surface capable of activating it. The methods employed yielded a more detailed picture of the pattern of localization within this region of the cortex than had yet been achieved by other methods including that of electrical stimulation of the cortex of conscious man.<sup>25, 41</sup>

The main facts already known for man were confirmed, but, in addition, certain new features were established, for example, the pre- and postaxial surfaces of the hindlimb were found to be represented, respectively, on the dorsal and mesial aspects of the hemisphere (Fig. 6, C). It proved possible to analyze the cortical map in terms of dermatomes<sup>57, 58</sup> and to show that the spinal segments from  $T_1$  through the last caudal ( $Ca_1$ ) are projected to the contralateral postcentral gyrus and paracentral lobule in the same serial order as that existing in the cord and with overlapping at the cortical level comparable in degree to that seen in the corresponding dermatomes. The serial order of the cervical segments is retained, but on projection to the cortex these segments are reversed en bloc. This reversal brings the cortical fields of the upper cervical segments in contiguity with the cortical fields of the upper thoracic segments, and places the cortical field of  $C_8$  adjacent to that of the trigeminal nerve. The reversal accounts for the fact that hand and face areas join in the cortex and

The story is essentially the same for the cat (Fig. 6, B). The chief differences are the somewhat larger size of the area in cat and a correspondingly greater spatial differentiation within the area for different portions of the body. There is no overlap, for instance, between face and hindlimb subdivisions.

In the monkey the area is somewhat larger still (Fig. 6, C). Its arm and leg subdivisions lie on the superior bank of the sylvian fissure. The face subdivision lies in part within the sylvian fissure and in part on the inferior parietal gyrus adjacent to the face subdivision of somatic I. Again face I and face II are distinguishable by latency differences and by the detailed pattern of representation in area I. Somatic area II responses are obtainable in the monkey only under quite light anesthesia, therefore it has been difficult to work with complete satisfaction on this animal. In this respect, too, the contrast with somatic I is great. Probably because of the suppressing effect of the anesthetic agent on somatic II responses it has not been possible as yet to demonstrate representation for trunk and proximal parts of the limbs in monkey. At first<sup>54</sup> we obtained responses only from the contralateral limbs. In this our first results on monkey resembled those of Adrian on cats,<sup>1, 2</sup> the limited nature of which may also be ascribed to depression by the anesthetic.

In the sheep and the pig most of the characteristics of somatic II already described for other species also have been established. As in monkey, responses from proximal parts of limbs and from trunk were small or absent, but both sides of the body were found to be represented in each hemisphere. With respect to differentiation of face, arm, and leg subdivisions, pig and sheep appear to take an intermediate position between rabbit and cat, if one may judge by the degree of overlap between subdivisions.

The ipsilateral face area has been found in all the animals studied in this laboratory (rabbit, cat, dog, pig, sheep, and monkey). In all of them it receives impulses from the same parts of the body, that is, from the lips, the lower side of the face, the tongue, the buccal cavity, and perhaps the pharynx. In all species it lies adjacent to an ipsilateral motor area for the same portions of the body (rabbit,<sup>16</sup> cat,<sup>27, 53, 56</sup> sheep,<sup>9</sup> monkey.<sup>56</sup> An ipsilateral motor face area similarly situated has also been reported for the goat.<sup>19</sup> In the monkey the ipsilateral motor face area lies at the lower end of the central sulcus on the precentral gyrus. In our own experiments<sup>56</sup> this area in the monkey was strictly ipsilateral but merged anteriorly and medially with the contralateral motor face area through a transition zone giving bilateral contractions. It may be noted that bilateral motor responses for the lower face have been reported for primates by several workers.<sup>24, 32, 33, 50</sup>

It is of great interest that those portions of the body which animal experiments have shown to be represented in the ipsilateral sensory and motor face areas are the parts of the body which have most often shown bilateral relations to the cortex in electrical stimulation of the brain of man.<sup>25, 41</sup> Penfield and Boldrey<sup>41</sup> (p. 440) reported bilateral sensations from lips, tongue, and mouth and bilateral movements of these same parts. They comment: "This bilateral response is in such striking contrast to its complete absence in the extremities that it must indicate a small degree of true representation of bilateral function

in each hemisphere.' From our own finding that the ipsilateral sensory area lies chiefly within the central sulcus in monkey and from the fact that much of the motor area in man is within the central sulcus, it seems likely that truly ipsilateral sensory and motor face areas in man may be largely buried on the walls of the central sulcus. The bilateral results described for man, then, would correspond to the results observed by us while recording from or stimulating the transition zones between contralateral and ipsilateral areas.

Dr. Dandy<sup>20</sup> has reported that ipsilateral sensory and motor functions in the domains of the trigeminal and facial nerves may be preserved in part after unilateral removal of one cerebral hemisphere in man. Possibly the ipsilateral areas just discussed have something to do with the preservation of these functions. One can scarcely account for the findings on the basis of somatic area II because arm and leg, as well as face, are bilaterally represented in this area.

What aspects of cutaneous sensory function are mediated by somatic area II is as yet unknown. A slowing of sensorimotor reactions (tactile placing) is the only impairment which has been observed to date following its unilateral removal in cats and monkeys.<sup>12</sup> We also know that somatic area II cannot compensate for loss of somatic area I in control of tactile-placing reactions.<sup>12</sup> Some recent interesting observations by Bender<sup>13</sup> on war injury cases, which he explains on the basis of bilateral cortical representation of the extremities, may prove related to somatic area II.

We have noted earlier in this paper that there are dual cortical areas not only for the somatic but also for the visual<sup>45, 48</sup> and the auditory<sup>49, 50</sup> systems (Fig. 6). Duality, therefore, appears to be a general principle of cortical organization. The position of somatic and auditory areas II between the rhinencephalon and insula on the one hand and the more highly differentiated areas I on the other suggest that the "second" areas may be phylogenetically more ancient and primitive. But the principle of dual representation is not limited to the cerebral cortex. This is clear from the study of Snider and Stowell<sup>44</sup> on afferent systems to the cerebellum. They found that tactile stimulation gave rise to electrical responses both in the anterior lobe and in the paramedian lobules. In the anterior lobe the responses are produced by ipsilateral stimulation only, while responses in one paramedian lobule can be evoked by stimulation of either side of the body, ipsilateral responses being larger than contralateral ones. These results suggest a parallelism between the anterior lobe and somatic area I, and between paramedian lobule and somatic area II. Indeed, Adrian<sup>5</sup> has shown that face, arm, and leg subdivisions of the rolandic cortex are related to face, arm, and leg subdivisions of the anterior lobe, and one of us (C. N. W.)<sup>56</sup> has found that somatic II and paramedian lobule are mutually interrelated.

One may deduce that undoubtedly separate pathways in the spinal cord serve these dual systems of the cerebral cortex and cerebellum. Possibly the systems concerned are those discussed by Brouwer.<sup>17</sup> If this is true then one must ask: Are there also dual systems of fibers in cutaneous, auditory, and optic nerves? It is tempting to think that this is so. We know that there are two types of auditory nerve fibers, the radial and the spiral. Do these respec-

tively project their messages to auditory areas I and II of the cerebral cortex? There are also the rods and the cones of the retina and two known types of vision, photopic and scotopic. Is photopic vision served by visual area I and scotopic vision by visual area II? (See Parsons<sup>40</sup> on dyseritic and epicritic visual systems.) Finally, one may recall that Head<sup>31</sup> postulated a dual system of cutaneous nerve fibers to account for phenomena associated with regeneration of peripheral nerves. It would be unwarranted to suggest a relationship between the dual cortical somatic systems and Head's postulated dual system of peripheral nerve fibers. Yet it is stimulating to think about this possibility, particularly since the detailed localization in somatic I and the less detailed localization in somatic II suggest that the function of the postcentral gyrus (epicritic?) would be much more seriously affected by confusion in the distribution of regenerated peripheral nerve fibers than would the function of somatic II (protopathic?). These are questions which one need not consider in a speculative manner only. It is quite possible, we think, to answer them by experiment.

#### SUMMARY

1. The somatic receiving areas of the cerebral cortex of pig and sheep have been studied by observing and recording the surface positive electrical potentials evoked in the cortex by mechanical stimulation of cutaneous receptors while the animals were anesthetized with pentobarbital sodium or with pentobarbital and chloralose.

2. As in other animals (rabbit,<sup>60</sup> cat,<sup>1</sup> dog,<sup>54</sup> and monkey<sup>54</sup>), two somatic afferent areas were found in each hemisphere: somatic area I, the homologue of the postcentral gyrus of primates and somatic area II, which in monkey lies on the upper bank of the sylvian fissure.

3. In both species an ipsilateral face area, receiving impulses from lips, side of face, tongue, palate and floor of mouth, also was found. This lies contiguous to and ahead of the contralateral face subdivision of somatic I. Whether it should be classified separately or as a part of somatic I has not been decided. Homologous areas have been found in cat, dog, rabbit, and monkey, and there is evidence that the ipsilateral face area may exist in man also.

4. In pig, face and arm subdivisions of somatic I were found; leg subdivision was not located but probably lies on the mesial surface of the hemisphere. In sheep, only the face subdivision of somatic I was studied.

5. Face, arm, and leg subdivisions of somatic II were demonstrated both in pig and in sheep.

6. In all animals so far studied the relations of cortex to skin are entirely crossed in somatic area I, with the exception of the ipsilateral face area. In the zone of transition from contralateral to ipsilateral face areas the relationships are bilateral.

7. Both sides of the body send impulses into somatic area II, but the contralateral responses are larger. Stimulations of snout, limb apices, and tail yield largest potentials. Few responses are produced by stimulation of trunk and proximal parts of the limbs, probably because the small responses to be expected (by analogy with cat and rabbit) are suppressed by the anesthetic.

8. Dual representation is not unique for the cortical somatic system. It has also been found in the visual<sup>45, 48</sup> and in the auditory areas<sup>49, 50</sup> of the cerebrum and in the tactile system of the cerebellum.<sup>44</sup> These dual systems provoke many interesting questions both for experimental and clinical investigation.

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## THE SURGICAL TREATMENT OF VASCULAR ANOMALIES OF THE PREMOTOR AREA PRODUCING EPILEPSY

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AT THE 1935 meeting of the Harvey Cushing Society I reported on the treatment of three patients with jacksonian seizures due to vascular anomalies in the premotor area. In this paper were discussed certain peculiar findings in the ventriculograms of separation of the bodies of the ventricles by angiomas, and the marked temporary paralytic reaction following the coagulation of abnormal cortical vessels. The paper was withheld from publication because less than five years had elapsed following the operations.

That same year in a report on epilepsy due to vascular abnormalities of the brain, sixteen cases of vascular abnormalities in which operation had been done during the previous six years were discussed. Of these cases, one was due to saccular aneurysm coagulated successfully, another to an arteriovenous aneurysm treated by decompression,<sup>1</sup> another to vascular occlusion of the aqueduct of Sylvius,<sup>2</sup> six to vascular anomalies of the premotor area, and seven to angiomas or hemangiomas.

In the fall of 1936, a third report of six cases of epilepsy with vascular anomalies in the premotor region was read at the Pan-Pacific Surgical Congress.<sup>3</sup> Emphasis was laid on (1) signs of the premotor syndrome or the signs of a combined motor or premotor lesion in these patients, (2) the fact that ventriculograms in three cases revealed a new finding of slight separation of the body of the lateral ventricles just posterior to the anterior horns, which was found to be caused by deeply situated angiomas in the callosal region, (3) the observation that four of the patients had dural angiomas besides cortical vascular abnormalities, (4) the disturbance of cerebral vascular balance by the coagulation of the anomalous cortical and dural vessels and angiomas resulting in marked cerebral edema and transient hemiplegia that disappeared with the development of adequate collateral circulation, and (5) the fact that the repeated use of intravenous hypertonic solutions proved a more satisfactory procedure than decompression or repeated ventricular punctures in controlling this postoperative cerebral edema.

It is now timely to review these experiences in attempting to treat epilepsy due to vascular anomalies located in the premotor area and to present case reports of fifteen such patients operated upon from 1935 to 1941, with at least a five-year follow-up period.

Although the paper is limited purposely to lesions of the premotor region, the reader is referred to the 1928 monograph of Cushing and Bailey<sup>4</sup> on blood vessel tumors of the brain, to the 1928 article of Dandy<sup>5</sup> on venous abnormalities and angiomas of the brain, and to Dandy's<sup>6</sup> chapter on the brain in *Lewis' Practice of Surgery*.

The importance of the frontal lobes has been emphasized particularly by the experimental work from the physiologic laboratories at the Yale University School of Medicine, where careful observations of the effect of stimulation and destruction of small areas in this lobe had substantiated the observations recorded in a few scattered clinical reports.

Following the localization of forced grasping in Brodmann's cortical area 6 in monkeys by Richter and Hines<sup>7</sup> in 1932, a physiologic evaluation of this area was made by Fulton, Jacobsen, and Kennard,<sup>8</sup> who, besides securing the involuntary grasping reflex, observed spasticity and increase in tendon reflexes on the side opposite to the lesion. Later Fulton and Kennard,<sup>9</sup> and Kennard<sup>10</sup> determined that a lesion in area 6 caused the dermal temperature of the contralateral side to be lower than the normal side and produced transient edema and changes in the color of the skin and diminished the production of sweat.

These experimental observations on the premotor area were applied to the problem of a patient on whom a surgical removal of a cystic glioma restricted to the right premotor area was performed, and led to the enunciation of the syndrome of the premotor cortex in man,<sup>11</sup> consisting of impairment of skilled movements, forced grasping, spasticity, vasomotor disturbances, and increased tendon reflexes. The advances in the study of this region during the past ten years have been compiled in a recent book on the premotor cortex edited by Paul Bucy.<sup>12</sup>

Although certain authors had advised no interference in patients with anomalous cortical vessels, the first two of the patients operated upon in 1935 presented a problem that seemingly might be attacked by coagulation of the aberrant vessels. The procedures used in handling the stormy postoperative course of these two patients made possible a smoother treatment of subsequent patients with similar lesions, both at operation and in the postoperative period.

Reports of most of the following cases indicate that these epileptic patients had the syndrome of the premotor area alone or in combination with the adjacent motor area, and in them the anomalous vessels found at operation were coagulated.

#### CASE REPORTS

CASE 1.—Mr. M. C., aged 21 years, was seen in January, 1935, because of fainting spells of two years' duration.

On Thanksgiving Day, 1932, he was pulling out blasted tree stumps. That evening, while at a dance, he developed nausea and severe headache and was found next morning drowsy, delirious, and with a right hemiplegia. Within three weeks the hemiplegia showed improvement, but the right foot was never restored to normal, remaining cold and stiff with the toes in an extended position.

In the ensuing two years he experienced six attacks in which he fell unconscious, with the extremities rigid in tonic contracture.

On examination, the reflexes were increased on the right with positive Babinski and Rossolimo signs and a sustained ankle clonus. The right foot was weak, and the toes were spastic, cold, and in an extended position. Ventriculograms showed slight dilatation of the roof of the left ventricle (Fig. 1).

A diagnosis of cortical cicatrix following a subarachnoid and cortical hemorrhage in the left motor and premotor areas, due to some vascular anomaly, was ventured and exploration advised.

A left craniotomy was performed Jan. 15, 1935, under avertin and local anesthesia. A localized subarachnoid laking was seen. A cystic area could be palpated in the motor leg area (Fig. 2). This was tapped at a depth of 1 cm. and 10 c.c. of clear, straw-colored, non-coagulable fluid were withdrawn. When the needle was passed through the cyst, resistance by firm tissue was encountered for a distance of 3 cm. Three abnormal arteries, appearing on the mesial aspect of the hemisphere, entered the cortex of the premotor area and, on lateral retraction of the cerebrum, a large vein with branches from the leg and premotor area descended on the mesial aspect to enter a large abnormal venous channel in the falx several centimeters below the longitudinal sinus. This was coagulated, as was a moderately-sized artery from the dura which entered the premotor area. In an attempt to tap the anterior horn of the left ventricle, arterial blood was obtained without any sensation being experienced that a vessel wall had been entered, therefore it was suspected that an angioma had been punctured. The needle was not withdrawn until bleeding had stopped. The bone flap was replaced and closure effected.



Fig. 1 (Case 1).—Anteroposterior view of ventriculogram showing slight dilatation of the roof of the left lateral ventricle from a subcortical scar.

On awakening from the anesthesia the patient had a slight aphasia and a right-sided weakness. A ventricular puncture gave 15 c.c. of clear fluid under moderate pressure.

During the course of the next two days the aphasia increased and the right paresis involved the hand more than the leg. Since it was feared that an extradural hemorrhage had developed, the bone flap was elevated under local anesthesia, January 17. A blood clot 1 cm. thick, which had formed beneath the bone flap, was removed. Because the dura felt tight,

although there was no subdural hygroma or hematoma, a subtemporal decompression was made. Subsequent ventricular punctures were planned, as well as a continuation of the limitation of fluid intake to 1 L. a day to control the edema.

Three right ventricular punctures, yielding 30 to 40 c.c. of clear fluid under moderate pressure each time, were made during the next day. No favorable response followed these taps and the patient became more drowsy, so on January 18 the bone flap was removed and preserved in alcohol for replacement later. Blood was again obtained at an attempt to tap the anterior horn of the left ventricle at this operation.

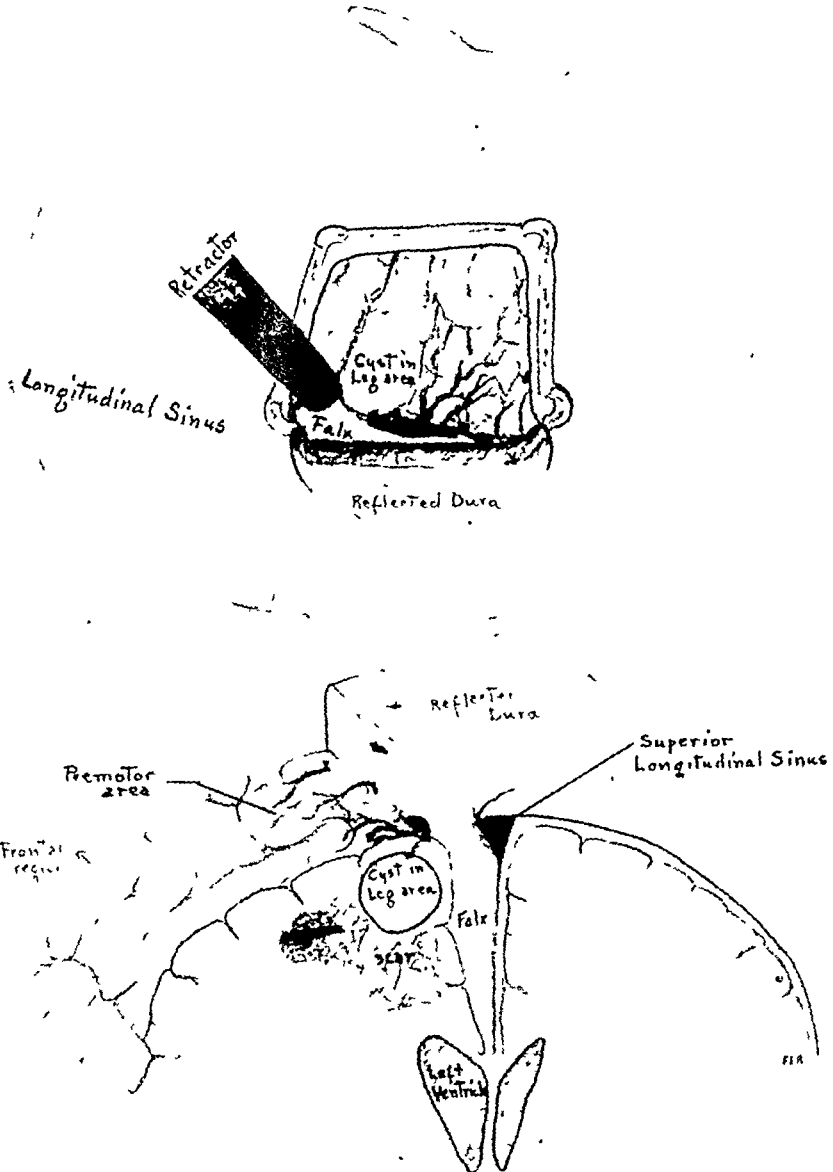


Fig. 2 (Case 1).—Operative exposure showing positions of cortical cyst, subcortical scarring, frontal angioma, and abnormal vascularity in left premotor region.

Further removal of right ventricular fluid by six punctures during the next day failed to make the patient more responsive, but after the intravenous administration of a hypertonic solution of glucose (12 per cent) and salt (5 per cent) a marked and favorable change was produced. The hypertonic solution was given twice daily for the next three days and, although a ventricular puncture was performed every six hours during the same period, it was felt that the deciding factor in his improvement followed the intravenous medications. By January 23 the decompression was soft, and rapid improvement occurred in the aphasia and right paresis.

An attack of influenza delayed his discharge from the hospital until February 9. At this time he showed a little hesitancy in speech with some weakness of the right upper extremity, and a more rapid recovery in the leg. The reflexes on the right were hyperactive with an ankle clonus and positive Babinski and Rossolimo signs. The spasticity in the right foot had disappeared and this limb was now as warm as the opposite one.

The patient returned on March 28, 1937, with a nearly normal gait, but a slight weakness and awkwardness still persisted in the right forearm and hand. Very little evidence of aphasia was found. The reflexes were still hyperactive but no pathologic reflexes could be obtained. The bone flap was replaced without any difficulty. The dura was under no tension. Only a few cubic centimeters of fluid were obtained in tapping the leg area. The cortex was not explored.

Since operation the patient has been examined on several occasions. The spasticity, coldness, and abnormal neurologic signs had disappeared, but he continued to have several epileptic seizures, clonic in nature, for three years, then occasional seizures in the next four years, with no seizures during the past three years. His speech was not rapid and the awkward, cold right upper extremity still was not much use to him as a grocery clerk.

*Comment.*—The onset of this lad's illness dated from Thanksgiving, 1932, when a subcortical hemorrhage, presumably from an angioma, occurred in the left premotor and motor areas. The cyst in the motor leg area, the subcortical cicatrix and angioma, revealed by operation, added support to this hypothesis. Abnormal arteries and veins in the premotor area, also disclosed by operation, were coagulated. An extensive cerebral edema developed postoperatively which was not affected by decompression, dehydration, and withdrawal of ventricular fluid, but was immediately and favorably influenced by the administration of hypertonic solutions given intravenously. Eleven years after operation found him with an awkward, cold, weak right upper extremity, slight evidence of motor aphasia when excited, and no seizures during the last three years.

CASE 2.—Miss L. P., a student, aged 25 years, was admitted in January, 1935, because of headaches, vomiting, and spasticity of the right hand for the previous ten days.

She had been subject to attacks of fainting for the preceding two years. In the first spell a friend noticed that the right hand and arm were spastically flexed. Subsequently she had transient periods of lightheadedness and headaches. By the fall of 1934 the headaches, usually occurring in the afternoon and found not to be due to eyestrain, were more frequent and severe, necessitating aspirin and barbital medication; the vertigo associated with nausea made her wonder if she had a brain tumor.

The recent episode came rather suddenly with nausea, vomiting, severe frontal headache, and spasticity of the right hand. She did not use the right hand because it was clumsy—she could not write with it. She complained of being dizzy, although objects did not move, and of having difficulty in walking. During a physical examination she paled and fell unconscious with tonic contraction of the right forearm and hand.

During the examination the patient was reticent in giving the history and kept her right hand under the covers. She was very despondent, with suicidal thoughts. Neurologically, hyperactive reflexes were found on the right side but there was no muscular weakness or

sensory change. The right hand was clenched but could be relaxed completely at times. Stroking the palm or pulling gently on the flexed fingers induced a marked spastic response. Her gait was unsteady and hesitant as the right leg was handled awkwardly and made her lurch to the right. Station was good, however. Touching the examiner's hand with her right foot or fingers was performed with hesitancy and inaccuracy. The right side of the body, especially the fingers and toes, at times felt definitely cooler than the corresponding part on the left side. The Babinski, Oppenheim, Hoffmann, and Rossolimo signs were negative. The eye grounds showed a slight haziness of the right nasal disc. The audiometer reading was normal. Blood pressure averaged 150/80, although two years before it was recorded at 120 systolic.

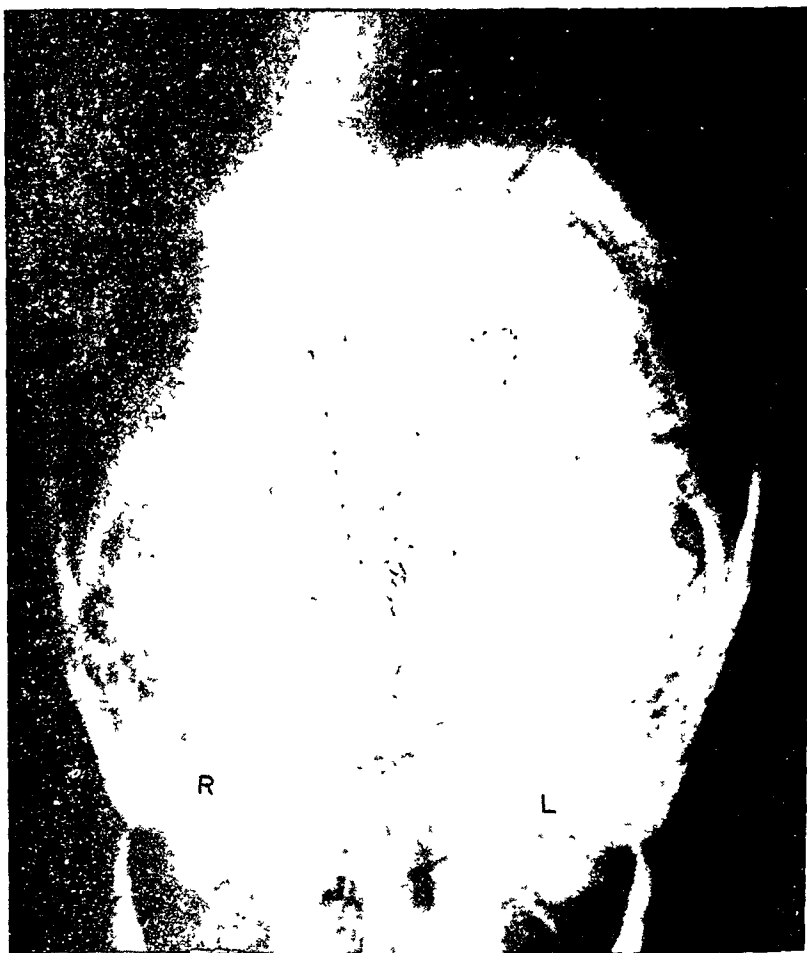


Fig. 3 (Case 2) — Anteroposterior view of ventriculogram showing slight separation of bodies of lateral ventricles

The tentative diagnosis of labyrinthitis was changed to either a left frontal tumor or vascular anomaly, and ventriculography advised.

The ventricular fluid was under increased pressure but the ventriculograms excluded a tumor of the frontal lobe since the ventricles appeared normal in size. There was, however, a slight separation of the bodies of the ventricles just back of the anterior horns (Fig. 3). A revised diagnosis of vascular anomaly in the left premotor area was offered.

A left craniotomy was performed under avertin and local anesthesia on March 2, 1935. The exposed dura contained a cavernous angioma (Fig. 4) several centimeters in diameter

and 3 cm. from the midline. On reflexion of the dura, seven arteries and veins were seen to extend from the dural angioma directly into the premotor cortex. There was a small area of subarachnoid laking with arachnoid opacity in this region. The cortex felt normal. The abnormal vessels from dura to cortex were coagulated, then the dural angioma was coagulated and excised. Fascia from the temporal muscle was used to replace the excised dura, and then the bone flap was replaced.

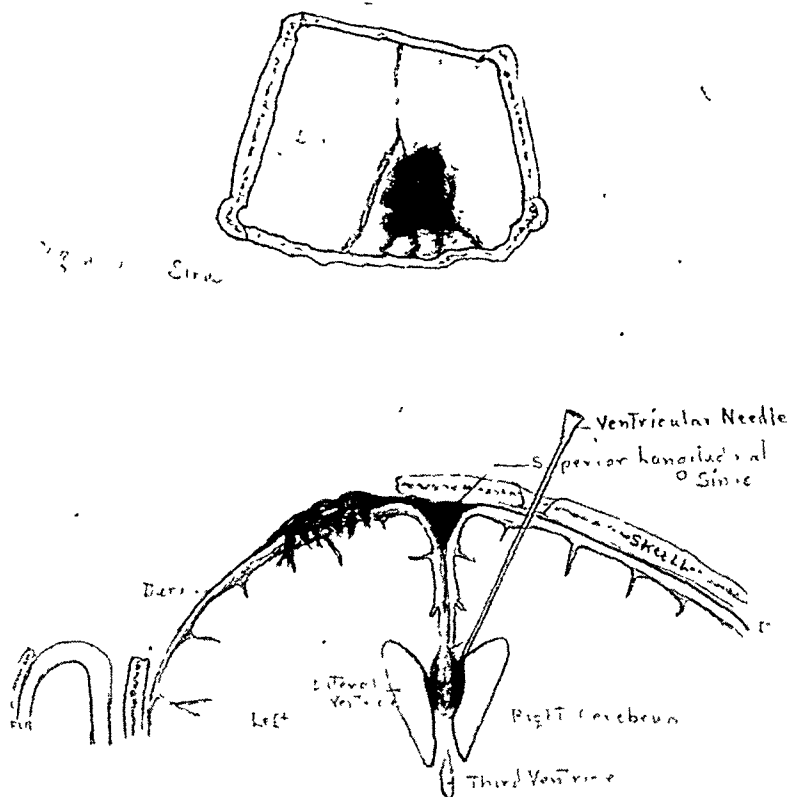


Fig. 4 (Case 2).—Operative exposure revealing the dural angioma with its seven arteries and veins entering the left premotor cortex, and the callosal angioma separating the lateral ventricles.

By evening the patient was awake, talkative, and without any right-sided weakness or spasticity, but the following day she was slightly drowsy. In view of the experience with the first case, ventricular puncture was done with the release of fluid under slight pressure. Intravenous injections of hypertonic solution of glucose and salt were given also, which made the patient more responsive. However, the second postoperative day found her drowsy and with



a definite right-sided paresis and aphasia which were not influenced by ventricular tap or hypertonic solutions to any marked extent, so a decompression was advised.

Before the bone flap was elevated, when an attempt was made to tap the right ventricle, through an anterior trephine opening, the needle encountered arterial blood without the operator feeling any resistance of a vessel wall. One ounce of blood flowed out briskly. By a slight shift of the needle, brain tissue came out which was pushed into the angioma by the stylet. This procedure caused a cessation of the bleeding and the needle was withdrawn. It was assumed that the needle's point had entered an angioma which had produced the slight separation of the lateral ventricles as shown by ventriculography. The bone flap was then elevated but only one-half ounce of clotted blood was found extradurally. As the dura was tight, a left subtemporal decompression was made.

The following two days showed an improvement in the patient's condition. Spinal instead of ventricular punctures were done, the fluid being slightly blood tinged, and hypertonic solutions were given intravenously twice daily. On March 6 the decompression was flat, the spinal fluid was straw colored, the blood pressure was around 125/75, and the patient was speaking a few words. The right hemiplegia persisted. The next day the left hand was spastic for short intervals, but this was never observed subsequently. The right hand also became spastic again, but relaxed the next day. Pain in the right arm and leg was a complaint, followed on March 10 by movements of the right toes. Rapid improvement in the aphasia and right hemiplegia persisted, but sitting up and walking was delayed until the fourth postoperative week because of annoying vasoconstriction when the patient was in the upright position, as shown by facial pallor and cold extremities, with the right hand becoming spastic. On reclining her color returned, followed by the warming of her hands and feet and relaxation of the right hand.

By the sixth week the aphasia had cleared, she could use her hand for eating and writing, and she walked with slight support. The reflexes were hyperactive on the right side, with an unsustained ankle clonus but negative Babinski, Oppenheim, and Rossolimo signs.

The vasomotor disturbance disappeared about the fourth week after operation, when the decompression was slightly sunken and she could perform the finer coordinating movements of the right hand, write legibly, and walk without support. Occasionally the right foot felt a little cooler than the left, but the hands showed no difference in temperature. The systole blood pressure stabilized around 120 since the first postoperative week.

After three months all signs and symptoms had subsided and an adequate collateral circulation apparently had developed.

About one year later, however, she experienced two fainting spells and then, rather suddenly, developed dizziness, nausea, awkward gait, a left sixth nerve palsy, and slightly elevated blood pressure. Conjugated deviation of the eyes to the left was noted a number of times. Leakage from the midline angioma was postulated and in the course of two months, without any particular treatment, the symptoms and signs disappeared and she returned to her classes.

In 1938, the patient married, the first child was born in 1940, and subsequent children in 1941, and 1943. Her neurologic examination has remained negative, and there have been no seizures since operation.

*Comment.*—In this young woman, signs and symptoms such as attacks of unconsciousness when the right hand was spastic, headaches, vertigo, nausea, and vomiting, with recent development of spasticity and forced grasping in the right hand which, at times, was cooler than the left, and hyperactive reflexes on the right side, gave the localization of a lesion to the left premotor area. The presence of a tumor was eliminated by the ventriculograms, although a slight separation of the lateral ventricles in the anteroposterior view was noted. Exploration revealed an angioma in the dura from which arteries and veins entered the premotor cortex. Another angioma in the callosal region was found

by needle puncture, which explained the separation of the ventricles seen in the ventriculograms, and its leakage one year later explained the bizarre bilateral symptoms.

Coagulation of the dural angioma and its abnormal vessels to the cortex produced an extensive left cerebral edema which caused drowsiness, aphasia, and hemiplegia that was not affected by withdrawal of cerebrospinal fluid or intravenous medication of hypertonic solutions. Following a subtemporal decompression, further withdrawal of spinal fluid, and particularly the administration of hypertonic solutions intravenously led to a rapid improvement. As collateral circulation developed, the signs of an irritative lesion in the premotor area gradually subsided. Eleven years later she showed no residual neurologic signs and has had no seizures since operation.



Fig 5 (Case 3).—Anteroposterior view of the ventriculogram showing slight separation of the bodies of the lateral ventricles and slight dilatation of the roof of the right ventricle.

CASE 3.—J. E., male, aged  $3\frac{1}{2}$  years, was admitted April 15, 1935. One year previously he had spells of falling and becoming rigid. They were momentary and without loss of consciousness. If he were eating at the time he would drop the spoon and cup from his left hand. Since infancy he was inclined to use his left hand but was being trained to eat with his right hand. A slight stutter in his speech was noticed, with some hesitancy in his words. By November, 1934, he was having twenty to thirty attacks a day of falling forward, his face being flushed on arising, with dilated pupils. The seizures were more fre-

quently early in the morning. In February the physical examination was negative. He was placed on a ketogenic diet and  $\frac{1}{4}$  gr. of phenobarbital twice daily which led to a marked diminution in the number of attacks and altered them to the extent that only nodding of the head was noticed. In March, however, the attacks of falling recurred and, on April 2, he had a convulsion in which he fell unconscious with clonic movements of the hands. His speech was indistinct for a short while after this seizure. Phenobarbital was increased to  $1\frac{1}{2}$  gr. daily. The roentgenograms of the skull and gastrointestinal tract were negative. No vestibular responses to caloric tests were found from the right vertical or horizontal canals, but there was vigorous response after douching the left ear.

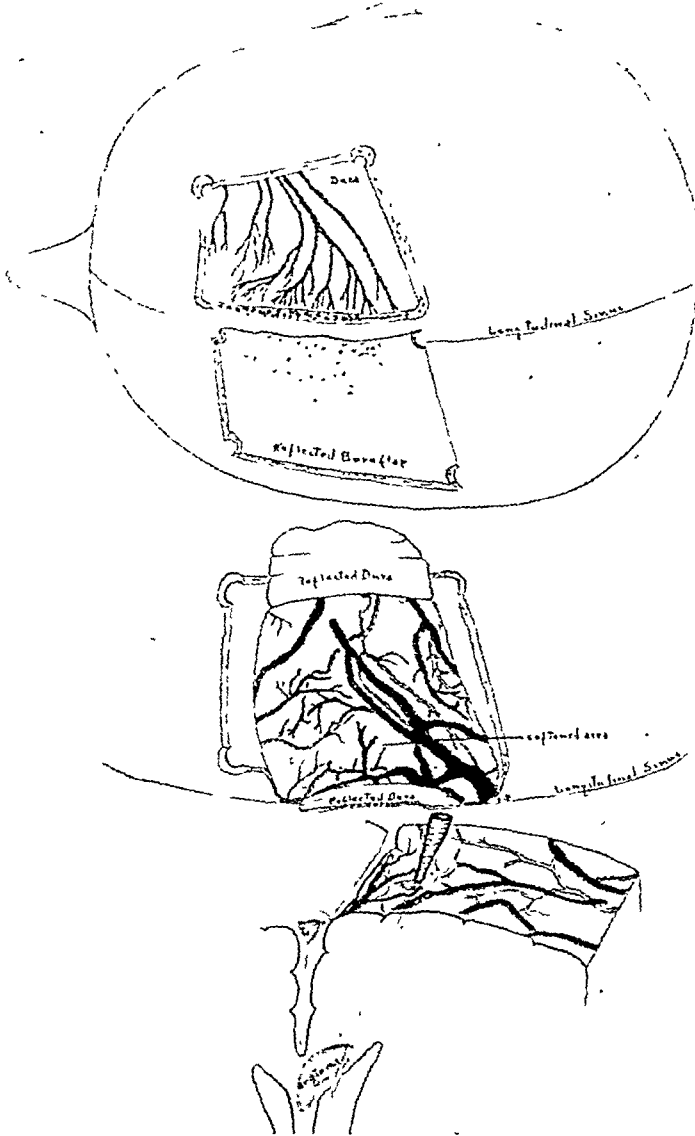


Fig. 6 (Case 3).—Operative exposure showing abnormal dural and cortical vascularity in right premotor region, the softened area; and the callosal angioma separating the lateral ventricles.

Examination on April 15 showed a very restless child with a tendency to stutter and to hesitate on simple words. He used both hands equally well. He sought his mother's hand in walking but when unsupported there was a tendency to throw out the left foot in a slow gait. While being examined his face flushed and he fell forward, striking his head against the crib, but he immediately arose crying and rubbing his head. The eye grounds showed nothing abnormal. The reflexes on the left side, particularly in the leg, were more active than on the right. Fanning of the left toes appeared on stroking the sole and Hoffmann's sign was positive on the left. The extremities had the same dermal temperature. A lesion, probably vascular, was suspected in the right premotor area and encephalograms advised.

Spinal air injection on April 16 showed small ventricles with bilateral absence of occipital horns. The subarachnoid channels did not deviate from normal. In the antero-posterior view the body of the right ventricle was a little larger than the left, particularly in the roof, and the lateral ventricles were separated just back of the anterior horns (Fig. 5), an appearance much like the ventriculograms in Case 2.

A diagnosis was made of vascular anomaly in the right premotor area, with a possible angioma in the callosal region separating the ventricles.

A right craniotomy on April 18 revealed the dura difficult to force from the inner table of the skull in the premotor region because of numerous branches of the middle meningeal artery entering the inner table. The bone was quite vascular along the longitudinal sinus. The abnormal, increased vascularity of the dura, however, did not extend into the cortex (Fig. 6). This portion of the dura was coagulated and destroyed. There was slight subarachnoid laking with a softened area palpable in the premotor region about 2 cm. from the midline. Just posterior to this area were rather large veins which formed a loose network close to the longitudinal sinus. Some of these veins were coagulated without causing any marked distention of the adjacent veins. A ventricular needle, introduced anterior to the softened area, was passed toward the ventricle. Blood slowly welled out, then, slightly deeper, cerebrospinal fluid was obtained. The needle was withdrawn until blood appeared and then the stylet was inserted in an attempt to put brain tissue into the angioma, which was situated between the lateral ventricles (Fig. 6). The bone flap was replaced and a right subtemporal decompression made.

The evening of the operation the patient's condition was good with no hesitancy in talking, or in the use of his left side, but the following day his speech was indistinct and hesitant. By the fourth day his speech was rapid and distinct. Slight twitchings of both hands were noticed at this time and the reflexes remained unchanged. A left jacksonian seizure occurred April 22. Suggestive athetoid movements of both hands, but more frequently on the left, were seen from the fourth to the seventh day. No spasticity and no forced grasping were noted.

In September, petit mal attacks became frequent with ataxia, increased reflexes on the right side, and bilateral Babinski and Chaddock signs. The decompression was full. An extension of the midline angioma seemed to explain the signs but, on repetition of the encephalograms, the same findings were obtained as before operation. Following this procedure the decompression became sunken and the spasticity and increased reflexes disappeared. The spells were less frequent, six occurring in three months, probably because he received  $3\frac{1}{2}$  gr. of phenobarbital daily. He accidentally took an overdose of barbitol and died in June, 1937, a little more than two years after operation.

*Comment.*—The unusual type of seizures in this child of 3 years, occurring more frequently in the morning and associated with flushing of the face, at times with contractions of the left hand and with transient speech difficulty, together with the findings of increased reflexes on the left, fanning of the toes, and a positive Hoffmann sign as well as separation of the lateral ventricles and slight dilatation of the roof of the right ventricle shown in the encephalograms, suggested the diagnosis of a vascular anomaly of the right premotor area with

a probable angioma in the callosal region. This was confirmed at operation. A right subtemporal decompression seemed to make the convalescence smoother. However, transient aphasia, twitching of the fingers with athetoid movements, and a few left clonic seizures indicated that the cauterization of the dural vascularity and of several abnormal cortical veins, and the needling of the callosal angioma had disturbed the abnormal vascular balance. Some months later (as in Case 2) leakage from the callosal angioma gave signs of bilateral involvement.

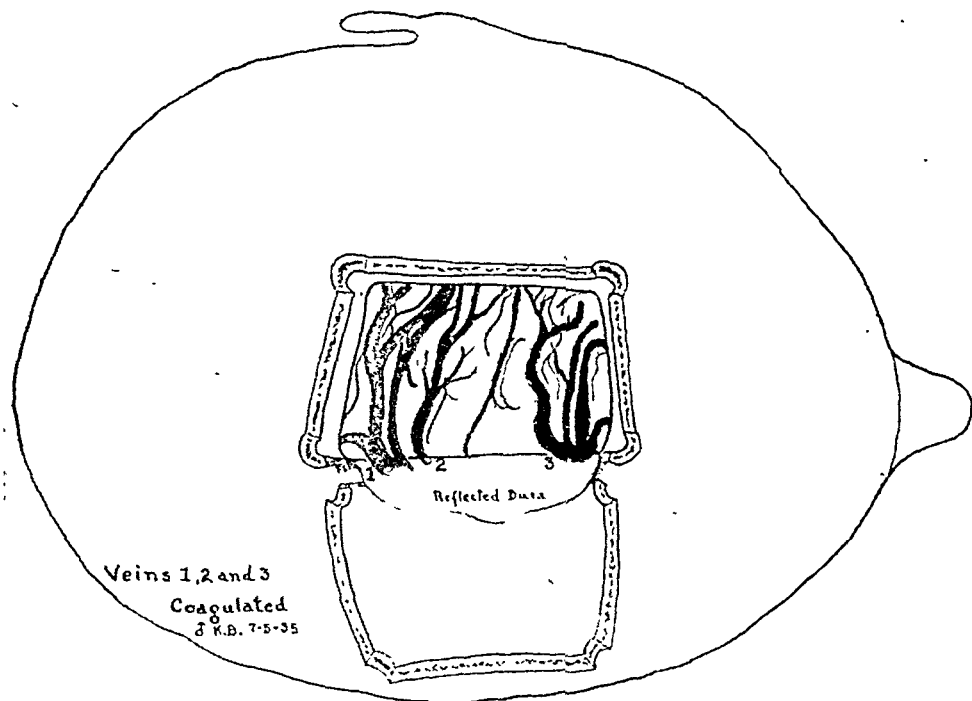


Fig. 7 (Case 4).—Operative exposure showing two groups (1 and 3) of large abnormal veins entering angiomas of the dura.

CASE 4.—K. B., male, aged 13 years, was admitted in July, 1935. Two weeks after a severe blow on the head, in January, 1933, he had a nocturnal seizure beginning with a sensation of a knife thrust in the right foot, followed by tonic contractions of the right ankle and knee, spreading up the right lower limb. During the attack he was pale and his feet were extremely cold. Three weeks after the sixth attack, in September, 1934, increased reflexes on the right with a positive Babinski sign and fanning of the toes were found. When the patient was examined eight months later these signs had disappeared.

A left craniotomy for a probable vascular anomaly was performed on July 5, 1935. Slight subarachnoid laking was seen, and a softened area was felt in the leg region. Two groups of large abnormal veins situated on either side of a small rolandic vein were seen to enter angiomas in the dura (Fig. 7). These vessels and the dural angiomas were coagulated and a subtemporal decompression made.

A transient aphasia and a right hemiplegia disappeared by the tenth postoperative day. A report one year later stated that he was entirely well and markedly improved in dis-

position. In July, 1945, ten years after operation, his sister wrote that he was "fine," had never had a seizure since operation, and was serving overseas as a radio operator in the United States Army.

*Comment.*—This vascular anomaly of the premotor cortex and dura, treated by coagulation, presented a fairly smooth convalescence probably because of the subtemporal decompression. No seizures occurred during the ten years since operation.

CASE 5.—E. W., male, aged 5 years, complained of dizziness and weakness since the age of 3 years. Shortly after the onset of the ataxic spells, he developed tonic flexor spasms of the right arm and wrist, as well as of the right face and leg. These spasms were likely to occur after playing or at night while he was sleeping. On examination the right side showed spasticity, forced grasping, and increased reflexes. Ventriculograms revealed slight separation of the bodies of the lateral ventricle, so that a diagnosis was made of a vascular anomaly in the left premotor area.



Fig 8 (Case 5) —Photograph of exposed left premotor cortex, the pointer indicating where cortical vessels were entering a dural angioma

A left craniotomy was performed on Aug 20, 1935. Many vascular communications from the premotor area entered a large dural angioma (indicated by pointer in Fig. 8). These vessels and the angioma were coagulated. Histologic study of the dural angioma showed it to be composed of vascular channels filled with blood. A subtemporal decompression was made.

A right spastic paralysis had cleared by the tenth postoperative day. Two weeks later tonic spasms recurred and still persisted two months after operation with the decompression remaining full. When examined April 5, 1937, one and one half years after operation, he had had no grand mal attacks and had not taken any phenobarbital. The spasticity of the right arm had disappeared two months after operation but when he was excited the right side of

the face contracted slightly and at night a small contraction of the right fingers might occur. Neurologic examination was negative. The last letter received (in September, 1937) reported him well and gaining in weight. The family has since moved and no further follow-up could be obtained.

*Comment.*—The premotor syndrome in this lad was found to be caused by abnormal cortical vessels entering a dural angioma. Coagulation of these vessels produced a temporary hemiplegia, but a smooth convalescence probably resulted from a subtemporal decompression. The last report, two years after operation, stated that he was well.

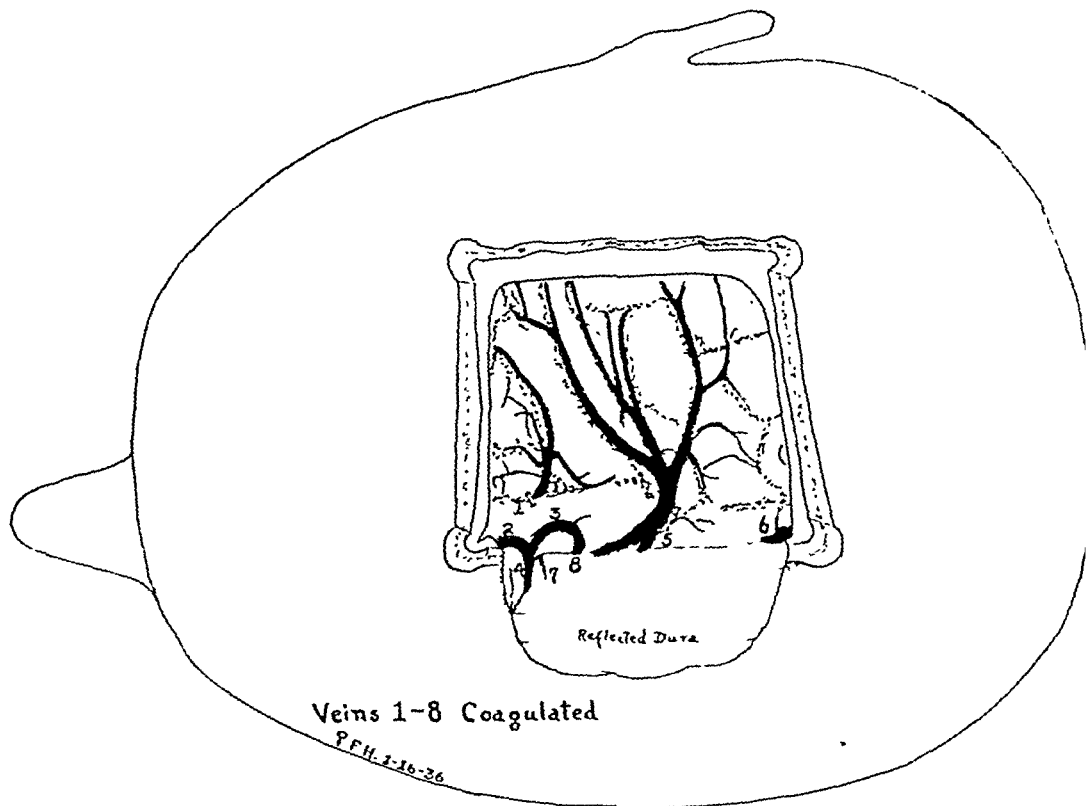


Fig. 9 (Case 6).—Operative exposure showing the many abnormal veins that were coagulated, including vein 5, that course beside the rolandic vein.

CASE 6.—Miss F. H., aged 24 years, was seen in May, 1931. An arrested hydrocephalus and a right torticollis had been present since childhood, possibly the effects of a difficult instrumental birth.

Illness at the time of admission dated from a fall in 1930, followed by weakness, heaviness, and awkwardness of the left arm and leg with, at times, dragging of the left foot. In 1931 the left hand and forearm were cold and spastic. Encephalograms showed a communicating hydrocephalus. In 1935 she dragged both feet, and both knees and legs were slightly spastic. Forced grasping in the left hand, and spasticity in the left wrist and elbow were demonstrated. Hyperactive reflexes, bilateral clonus, bilateral Babinski sign, and fanning of the toes were found. Both feet and the left hand were cold.

An irritative lesion in the right premotor area, probably a vascular anomaly extending over to the upper left premotor region, was diagnosed and a right craniotomy was performed on Jan. 16, 1936. No subarachnoid laking was seen. A large abnormal vein in front of area

6 ran from the cortex into the dura some 3 cm. from the longitudinal sinus. Silver clips were applied and the vein coagulated (Vein 1, Fig. 9). The rolandic vein was composed of three to five branches starting in the temporal region and uniting into a large trunk in the leg area (next to Vein 5, Fig. 9). In front of the ear two large tortuous veins entered the dura where they formed small angiomas. All the anomalous veins were coagulated, leaving only the rolandic vein. No subtemporal decompression was made.

The day after operation, spasticity was increased on the left side but with no increase in weakness. Spasticity and coldness were marked on the third and fourth days, but were gone by the ninth postoperative day. Five weeks later walking was improved, the limbs were warm, and spasticity and forced grasping were not demonstrated. Six months after operation pains developed in the left arm and elbow which became cold and spastic, with forced grasping and flexion contractures developing. In June, 1937, bilateral lumbar sympathetic block with alcohol warmed the lower limbs and slightly improved the spasticity of the lower extremities so that she could walk and climb stairs better. No further reports have been obtained from this patient.

*Comment.*—This girl had an arrested hydrocephalus from birth. Recent left-sided premotor symptoms and signs led to exploration and the coagulation of numerous abnormal veins, with only temporary relief.



Fig. 10 (Case 7).—Photograph of brain showing the left cortical atrophy in premotor area and the compensatory dilatation of the left ventricle.

CASE 7.—Miss M. L. N., aged 23 years, was admitted Dec. 7, 1936, because of convulsive seizures of two years' duration.

A congenitally deformed right foot prevented walking until the age of 4 years. When 10 years old she struck her head on a rock. On examination five months after the onset of seizures a diagnosis was made of Little's disease and jacksonian epilepsy, and treatment started of phenobarbital and a ketogenic diet.

The seizures began in April, 1934, with the right arm suddenly flexed, and with spasms of the right face spreading to the right leg. Occasionally the clonic seizures became generalized. The attacks were without aura and in some seizures she lost consciousness.



On examination the right foot was arched and everted, and the right leg was small and weak. The right arm was weak, with deformity of the fingers. The reflexes were hyperactive on the right side with a questionably positive Babinski sign.

Because of the Jacksonian seizures a left craniotomy was made on Dec. 12, 1936, at which time a cortical cyst was found in the parietal region. Anterior to the cyst the dura was adherent to the motor cortex. When the dura was freed a venous angioma was uncovered which was located, by stimulation, in the premotor arm and face areas. Several abnormal veins and the angioma were coagulated.

Following operation no aphasia or weakness developed. In February, 1937, Jacksonian seizures recurred but they were reduced to one or two a year under phenobarbital medication of  $\frac{1}{2}$  gr. twice a day.

In August, 1940, she attempted suicide with an overdose of phenobarbital and in November, 1940, she developed a lung abscess and empyema, refused surgical drainage, and died Nov. 7, 1940.

An autopsy showed multiple lung abscesses with empyema and a marked, localized unilateral left cerebral atrophy with compensatory dilatation of the left ventricle. The premotor area of the left frontal lobe particularly was affected (Fig. 10). Sections in this region showed a narrow zone of gray matter and beneath this were broad areas of glial tissue with scattered phagocytes containing granules of brown pigment.

*Comment.*—A birth trauma produced changes in the right arm and leg. Jacksonian seizures developed later on the right side. A cortical cyst resulted apparently from the birth trauma, although adjacent to it a cortical venous angioma was found and coagulated. Seizures recurred after operation. Four years later, autopsy showed cortical atrophy in the left premotor area.

CASE 8.—W. C., male, aged 10 years, was admitted to the clinic in April, 1937. In 1932, he had fallen a distance of eight feet, struck his head on a concrete sidewalk, and remained unconscious for several hours. He developed headaches, personality changes, and increasingly frequent and severe convulsions in which his eyes turned to the right, the right arm and leg drew up, and, finally, tonic contractions of all extremities developed. Immediately following a seizure the Babinski, Oppenheim, and Gordon signs were positive on the right side but, at other times, the neurologic examination was negative. Memory loss and a personality change indicated by disagreeable, impulsive, unreasonable, and cruel reactions made him a behavior problem. Encephalograms showed a small filling defect in the middle of the body of the left ventricle. Exploration seemed indicated because of an irritating lesion of the left motor cortex.

Operation was performed April 13, 1937. The premotor cortex had soft areas with many capillary vessels entering large cavernous veins that extended toward the longitudinal sinus. All of these large veins were coagulated, leaving only the Rolandic vein. Recovery was rapid without hemiplegia, and he was dismissed April 21. On April 25 he fell from a swing, disrupting the craniotomy wound which became infected, later necessitating removal of the bone flap. He was entered in the State hospital for behavior disorders and convulsions, where he remained until January, 1938, when he returned home so improved that he entered high school. Only two seizures occurred from 1937 to 1940, under dilantin, 0.1 Gm. three times a day. However, in 1944 and in April, 1945, he was arrested for stealing. His seizures have been much less frequent than before operation.

*Comment.*—This lad's condition seemed to have originated from trauma, yet the large abnormal vessels, resembling a hemangioma, of the left premotor cortex did not appear to have resulted from scarring.

CASE 9.—J. C., male, aged 10 years, was admitted to the clinic June 23, 1937, because of convulsions involving the left side of the face and upper extremity for two years.

This patient had been born two weeks prematurely and was a "blue baby" for several days.

Two and one-half years before entry he struck his head on a rock. Six months later the seizures started, usually at bedtime, with clonic movements of the left side of the face and neck occasionally progressing to the left arm. Encephalograms were normal. A diagnosis of a probable vascular anomaly was made.

Right craniotomy on June 26, 1937, revealed a small dural angioma over the upper part of the premotor area with cortical vessels entering it. These vessels and the angioma were coagulated. Palpation revealed a softened spot in the face area where a very large vein was also coagulated.

From the time of operation until the last report in March, 1941, he had had no seizures.

*Comment.*—Jacksonian seizures of the left side in this boy were caused by a vascular anomaly of the dura and cortex which was coagulated. He was normal with no convulsions during the four-year follow-up after operation.

CASE 10.—Mr. A. C., aged 20 years, was admitted Aug. 14, 1938, because of convulsions that began at the age of 13 years. These seizures started in the right hand, progressed up the forearm and arm, and then spread to the opposite arm. When the legs were involved in clonic contractions, consciousness was lost. Neurologic examination was negative except for sluggish mentality, with a slow speech.

A left craniotomy on Aug. 16, 1938, revealed numerous abnormal veins and arteries in the premotor area. On stimulation, these were found to be in the finger area. Just posterior to this vascular area a softened region, 2 cm. in diameter, was explored revealing a subcortical angioma, bluish in color, which blanched on pressure. A circumscribed coagulation gradually removed this angioma. The abnormal surface veins in the finger area were coagulated also. Pathologic study of the excised angioma showed it to be honeycombed by small branching endothelial-lined channels which were filled with blood, indicating a plexiform hemangioma.

Subsequent to operation, attacks without loss of consciousness occurred about once a month. During the war he worked as a stock clerk in a Naval Arsenal, the seizures being fairly well controlled by phenobarbital and dilantin. However, on the night of Sept. 1, 1945, he was found dead in bed, probably from a convulsion.

*Comment.*—Apparently, this patient's jacksonian seizures were caused by a cortical hemangioma in the premotor area. This was excised by coagulation. The convulsions after operation probably were initiated in the operative scar.

CASE 11.—D. C., male, aged 12 years, entered the hospital in September, 1938. His mother had had generalized convulsions for twenty-five years, since the age of nineteen years. The patient's seizures began four months before entry, with an aura of numbness in the left forearm, followed by clonic movements of the left upper extremity. Neurologic examination was negative except for a positive Babinski sign on the left side. Encephalograms, September 9, showed normal ventricles and subarachnoid channels, although roentgenograms indicated a rarefied region of the skull in the right hand area. A vascular anomaly was considered and exploration advised.

Right craniotomy, Sept. 12, 1938, exposed a thin and bulging dura beneath the rarefied region of the skull. When the dura was reflected the underlying cortex was raised irregularly with a few small cysts that were filled with either blood or dark brown material, suggesting a hemangiomatous tumor. Stimulation showed this to be in the hand area. This vascular tumor, 5 cm. in diameter, was excised by coagulation and the bed carefully fulgurated. Pathologic studies revealed a cavernous hemangioma with large thin-walled, endothelial-lined spaces filled with red blood cells.

Left-sided weakness with numbness developed after operation. By the end of October he could walk alone and could use his left hand. His reflexes were increased on the left side with a positive Hoffmann sign. The last examination, April 30, 1943, about five years

after operation, showed a weak left foot with unsustained ankle clonus, and an awkward but usable hand. He had had no convulsions since operation. Phenobarbital was discontinued two years after operation.

*Comment.*—This patient's jacksonian seizures were caused by a cortical hemangioma which was removed by coagulation. No convulsions have occurred since operation. He was left with a slightly weak foot in dorsiflexion and a clumsy but usable left hand.

CASE 12.—Miss M. D., aged 13 years, entered the hospital because of convulsions beginning at the age of 6 years. An aura of numbness and weakness in the left arm preceded the clonic seizures which started in the left upper extremity. By May, 1939, weakness in the left arm and leg had developed, gait was slightly ataxic, with positive Romberg sign and increased reflexes on the left side. Encephalograms in January, 1939, were normal. Electroencephalography in July, 1939, showed abnormal waves over the right motor area. Because of the long history of seizures, a preoperative diagnosis of possible vascular anomaly was made.

A right craniotomy on July 11, 1939, showed slight subarachnoid laking with a softened area which, on stimulation, was found to be the arm area. The large vein which entered this area was coagulated. Two centimeters above the arm area two large and several small veins entered the cortex from a small dural angioma. These veins and the angioma were coagulated.

Two weeks after operation the left hand was still weak. In September mild seizures, without clonus of the arm, recurred. In January, 1940, the seizures were frequent, and weakness and awkwardness of the left arm returned. Encephalograms made in March, 1940, showed the body of the right ventricle a little larger and higher than the left. By January, 1941, although still having convulsions, the patient had much better use of the left upper extremity.

In April, 1944, the left hand was used almost as well as the right. In the previous five months eight mild seizures occurred involving only the left upper extremity, and without loss of consciousness. She was married in 1944. It was reported in August, 1945, that she continued to have an occasional mild seizure while on a dosage of 1 gr. of phenobarbital three times a day.

*Comment*—A vascular anomaly in the premotor area was suspected in this girl because of the long history of jacksonian seizures and the recent development of left-sided weakness. Abnormal cortical veins from a dural angioma were coagulated. Mild jacksonian seizures still persist, although the left-sided weakness has disappeared.

CASE 13.—Miss R. R., aged 18 years, was admitted July 10, 1939, because of jacksonian seizures beginning with the onset of menstruation at the age of 14 years. The eyes rolled upward and to the right, then clonic seizures started in the right side of the face and spread to the right upper extremity and then to the right lower extremity, and often became generalized. Except for two or three attacks at each menstrual period, she was a normal, intelligent girl whose neurologic examination was negative. Electroencephalography gave abnormal waves without localization.

Left craniotomy, July 12, 1939, revealed a slightly thickened dura and considerable subarachnoid laking. In the area, identified by stimulation, supplying the face a number of small vessels, mainly arteries, entered a depressed region in the cortex. These arteries and one large vein were cauterized by electrocoagulation transmitted through a small cotton pledget.

Convalescence was smooth, with only a suggestive weakness of the right side of the face.

In August, 1939, a new type of seizure occurred on the opposite side, starting in the left side of the face with the left side of the body becoming rigid, while the right side re-

mained flaccid. These new convulsions continued through 1940 and 1941. In October, 1941, she deliberately became pregnant to cure her condition and had no seizures during the two months before a spontaneous abortion.

She re-entered the hospital in March, 1942, and electroencephalography still showed diffuse delta activity. Encephalograms revealed poor filling of the body and anterior horn of the right ventricle, with this ventricle and the third ventricle pushed 3 mm. to the left of the midline, suggesting a space-occupying lesion in the right frontoparietal region.

A right craniotomy on March 11, 1942, exposed a normal appearing cortex. Four explorations with a ventricular needle were negative. A subtemporal decompression was made.

A slight left paresis was present for two weeks and then disappeared gradually. Left-sided convulsions occurred occasionally, but finally ceased in October, 1943, and have not recurred for two years. She worked in a defense plant until her recent marriage, and she has taken no phenobarbital since 1943.

*Comment.*—Exploration revealed the apparent cause of the jacksonian seizures. Coagulation of abnormal vessels in the left area of the face stopped these right-sided convulsions. Shortly after operation, jacksonian attacks of the left side developed, and this condition led to a negative exploration of the right cerebrum three years later. The left jacksonian seizures became infrequent and have not occurred during the two years since October, 1943.

CASE 14.—Miss E. H., aged 15 years, was seen in December, 1939, because of peculiar attacks of abdominal pain occurring usually at night. These attacks started after an otitis media at the age of 5 years and were described by her mother as causing the child to cry out that her abdomen hurt. She would try to reach the bathroom, but usually became confused and lost. When she returned to bed the epigastric cramp might continue and she would have chewing motions of the mouth, and chilly, shaking limbs. She always urinated following an attack. The attacks became worse in the fall of 1939, five to twenty occurring in a month. Some were in the daytime, with a hot sensation, especially in the neck region, awkwardness of the left hand, and then an aching in the epigastrium which became cramp-like. Before an attack she was likely to have a voracious appetite. Following an attack she became pale and cold, and frequently had headache and nausea. Recently, with the epigastric pain, large white spots appeared on the left leg and disappeared when the pain ceased.

In 1936 appendectomy was performed for the cramps, and a recent gastrointestinal series and gall bladder visualization proved normal. Phenobarbital and low fluid intake did not affect the attacks. The reflexes were increased on the left side, with awkwardness of the left hand and foot.

Encephalograms in March, 1940, showed slight compression of the lateral wall of the body of the right ventricle without any shifting of the ventricle.

A right craniotomy on June 3, 1940, revealed a cortex covered with abnormal arteries and veins. No sylvian artery was seen but there were many small arteries in this region. At the upper end of the sylvian fissure, four large veins coalesced into a huge vein as it approached the base of the brain. After a hiatus in the face area, seven veins from the cortex extended upward and forward to the longitudinal sinus (lower left in Fig. 11). Slight sub-arachnoid laking was noted, except in several areas where the brain felt soft. Since sub-cortical angiomas were suspected, two of these soft areas were explored through a small nasal speculum but no angiomas were encountered. A spider web of abnormal vessels, mainly veins, was coagulated directly in front of the hand area (center in Fig. 11), some 3 cm. anterior to the rolandic fissure.

Epigastric pain and occasional spells continued until December, 1940. Then for one year she was free of attacks. In December, 1941, epigastric aching, with white areas on the left leg, returned, but the awkwardness of the left arm and leg was gone. In 1943 she had



Fig. 11 (Case 14).—Photograph of the exposed right premotor region showing the spider web of abnormal vessels in the center of the photograph located in the hand area, and the two groups of veins coursing forward to the longitudinal sinus.

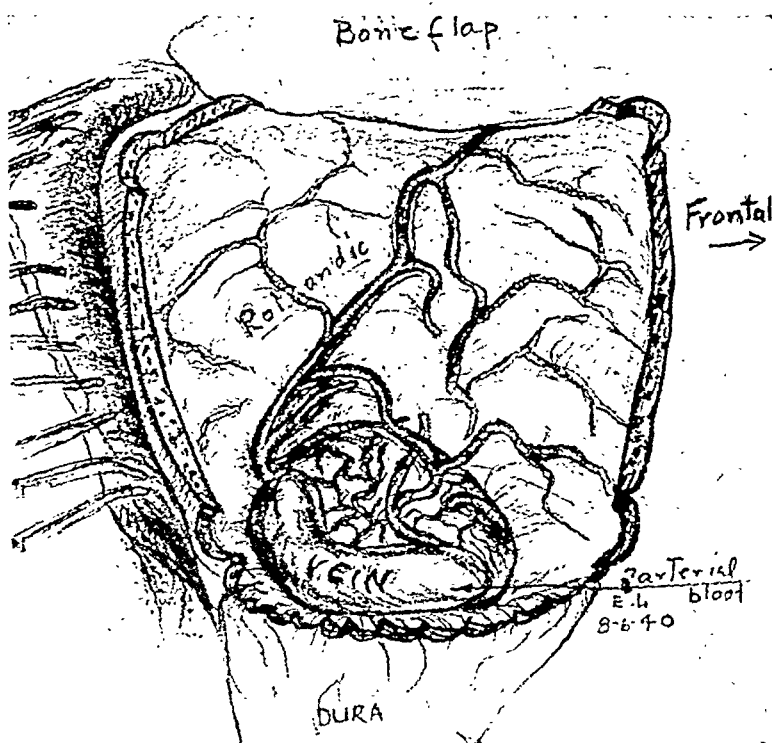


Fig. 12 (Case 15).—Operative exposure showing the large left cortical angioma that was coagulated two-thirds of the way around to stop pulsation.

eleven spells; in 1944, twenty-one spells; and in 1945, nineteen spells still characterized by crying out because of epigastric pain, "chilly" shaking of limbs, and urination. The white spots on the left leg have not appeared in the last two years.

*Comment.*—These attacks of epigastric cramps, with chewing motions of the mouth, and with white areas of skin appearing on the left leg, associated with increased reflexes on the left side and clumsiness of the left extremities, indicated a right premotor lesion. Abnormal cortical vascularity in front of the hand area was found and these vessels were coagulated. Improvement in the awkwardness of the left side and cessation of vasomotor blanching of the left leg followed operation. However, one or two mild spells a month of epigastric pain associated with shaking of limbs and urination occurred five and one-half years later.

CASE 15.—Mr. E. L., aged 24 years, was admitted in August, 1940, with a history of three jacksonian seizures during the previous two months. The attacks began in the right arm, where a numb feeling was followed by uncontrolled clonic flexions of the right forearm, which spread to the other extremities, and unconsciousness. The neurologic examination was negative. Roentgenograms showed the pineal body in normal position. Electroencephalography was reported normal but on review, after operation, prominent pulse waves were found in the center and to the left in the parietal region.

Left craniotomy on Aug. 6, 1940, exposed an unusual nest of veins in front of the rolandic fissure (Fig. 12). This pulsating angioma was 6 cm. in diameter and was composed of veins fully 1 cm. in diameter with numerous small arteries entering from the frontal region. This mass of vessels was tied or clipped and coagulated for two-thirds of the way around until pulsation could not be palpated. The destruction was carried inward for 2 cm. The angioma was not excised because it extended into the rolandic fissure and because of considerable bleeding. Fifteen hundred cubic centimeters of blood were transfused.

When the patient was dismissed, August 27, the right hemiplegia and motor aphasia were still present. By October, he could speak quite well and could move the right side, but could not walk well until the spring of 1941, at which time he could hold objects in the right fingers and hand. In September, 1941, when he returned to work in a service station, he had a slight limp and a spastic arm.

He was examined last in May, 1943, and there was no evidence of aphasia. The right arm and hand were usable but awkward, and were cool. The right leg was strong with a slight outward swing on walking. Phenobarbital,  $\frac{1}{2}$  gr. three times a day, has kept the seizures down to one to three a year.

*Comment.*—Although the large angioma which produced the jacksonian seizures was not removed completely by coagulation, apparently it has not recurred, and the occasional seizures were attributed to reaction to scar tissue.

#### SUMMARY

This report of fifteen cases of premotor vascular anomalies causing jacksonian epilepsy which were treated by coagulation of the vascular lesions during the six-year period, from 1935 to 1941, indicates that the operative procedure was feasible and satisfactory.

Nine of the fifteen patients had premotor signs.

Six of the fifteen patients, besides having the cortical vascular anomalies, had one or more dural angiomas.

Four of the fifteen patients had cortical angiomas or hemangiomas.

In three of the fifteen patients callosal angiomas were proved by ventricular needle puncture.

In these three callosal angiomas the ventriculograms showed a new sign of separation of the bodies of the ventricles.

Coagulation of the abnormal vessels frequently produced a transient hemiplegia, until normal collateral vascular channels developed.

Subtemporal decompression made a smoother convalescence if employed when there was evident disturbance of cortical circulation resulting from coagulation.

Intravenous hypertonic solutions aided materially in overcoming the cerebral edema that followed the disturbance of circulation incident to the operative coagulation.

Two of the fifteen patients had only temporary relief from seizures, after operation.

Seven of the fifteen patients had milder and less frequent attacks following operation.

Six of the fifteen patients, or 40 per cent, had no seizures after operation.

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# THE IMPORTANCE OF AIR STUDIES IN A NEUROSURGICAL CLINIC

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THE introduction of ventriculography<sup>1</sup> and of encephalography<sup>2</sup> by Walter E. Dandy in 1918 and 1919, respectively, may be said truly to have inaugurated a new era in the investigation of diseases within the skull. It is, indeed, quite impossible to overemphasize the importance of these studies or to make anything like an accurate estimate of the lives they have saved or the discomforts they have relieved. If one considers air studies from the aspect of brain tumors alone, it is at once apparent how much this diagnostic measure has meant in the preservation of life. Before the era of ventriculography it was estimated variously that from 50 to 60 per cent of all brain tumors could be localized with sufficient accuracy to be disclosed at operation. By the use of air in the ventricles it has been possible to demonstrate the situation of practically all of the previously unlocalizable 40 to 50 per cent of intracranial growths. This means that by this single diagnostic measure nearly one-half of the total number of patients suffering from brain tumors are capable of having the tumors found at operation, and since we know that roughly 50 per cent of all intracranial neoplasms are capable of complete removal once they have been disclosed, the importance of air injections in brain tumor surgery is at once apparent.

It was perhaps quite natural that this type of investigation should have been taken up slowly by neurologic surgeons during the first few years after the announcement of the procedure had been made. This was due partly to the conservatism which most surgeons felt in regard to what might be the effect of air within the brain, but also to the fact that early experiences in some clinics had been followed by severe reactions and an occasional death. It was soon appreciated, however, that if the operation for removal of the tumor was undertaken immediately following the air injection, these difficulties did not result.\* With this fact established, the value and importance of Dandy's discovery became manifest and with each succeeding year the employment of cerebral air studies increased enormously. The purpose of the present communication is to furnish an idea of the great usefulness of such studies in a neurosurgical clinic during the course of a single year.

At the Lahey Clinic from May 1, 1944, to April 30, 1945, a total of 429 cerebral air studies was carried out. Of these, 323 were encephalograms and 106 were ventriculograms. By ventriculography is meant the direct injection of air into the cerebral ventricles after making burr openings in the skull. Encephalography is the introduction of air (or oxygen) into the spinal subarachnoid space and thence to the cerebral subarachnoid spaces and ventricles by means of a

\*In the present series of 429 patients subjected to air study there were 3 deaths. Two of these occurred following encephalography in defective children with marked internal hydrocephalus due to cerebral birth injury, and the other in a stuporous patient with brain tumor, following ventriculography before the immediately planned craniotomy could be well started. The total mortality, therefore, was 0.7 per cent.



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In these three callosal angiomas the ventriculograms showed a new sign of separation of the bodies of the ventricles.

Coagulation of the abnormal vessels frequently produced a transient hemiplegia, until normal collateral vascular channels developed.

Subtemporal decompression made a smoother convalescence if employed when there was evident disturbance of cortical circulation resulting from coagulation.

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CASE 2.—J. V. T., a 40-year-old man, was admitted to the New England Baptist Hospital on Jan. 19, 1945. The chief complaints were headaches and dizziness. The former had become severe during the three months previous to admission, although they had been present for two years. Dizziness had been noted at intervals for one year.

Neurologically there were no positive findings other than bilateral papilledema of 2 to 3 diopters. A ventriculogram was performed on Jan. 22, 1945, and this disclosed normal-sized ventricles which were in no way displaced. For this reason a right subtemporal decompression was carried out in order to relieve the pressure symptoms and choked disks. He was discharged on Jan. 31, 1945. On Oct. 9, 1945, he reported for the most recent checkup examination. The decompression area was soft and the fundi were within normal limits. He had had only occasional slight headaches, and had resumed his former job several months previously.

*Comment.*—This patient represents a well-known class of individuals who have evidences of increased intracranial pressure and are suspected of having a brain tumor. The latter, however, can be ruled out only by demonstrating a normal ventricular system by the use of air. The underlying condition is probably an arachnoiditis or meningo-encephalitis.

2. *To Localize a Brain Tumor When Neurologic and Other Data Gave No Indication of Its Site.*—An excellent example of such a tumor is illustrated by Case 3.

CASE 3.—I. B., a 31-year-old married woman, was admitted to the New England Deaconess Hospital on May 4, 1944. She had complained of frontal headaches for nine months. These had been persistent until two weeks before admission when they had ceased. At times she had had mild nausea and periods of momentary blindness, but no other subjective symptoms.

Neurologic examination disclosed bilateral choked disks of 4 diopters with considerable new tissue formation embedding blood vessels over the disks. Venous tortuosity and engorgement were marked. There was questionable weakness of the lower left side of the face and, curiously enough, some question of sensory loss throughout the whole right side. Visual fields were normal.

On May 6, 1944, a ventriculogram showed displacement of both lateral and third ventricles to the left, with displacement backward of the right frontal horn as well. A right frontal craniotomy was performed the same day and an extensive soft glioma occupying the whole right frontal lobe and the anterior portion of the temporal lobe was radically but subtotally extirpated. Pathologically, the tumor proved to be a fibrillary astrocytoma.

The patient made a good recovery and was discharged on May 27, 1944. She was very well and resumed all her usual activities for sixteen months, when she again began to have intracranial symptoms. She was reoperated upon on Nov. 21, 1945, and the recurrent growth once more cleaned out. She has made a good recovery from this secondary operation.

3. *To Locate the Site of a Tumor More Exactly, Even Though Certain Localizing Evidences Were Present or When False Localizing Signs Happened to Exist.*—The third point is an extremely important function of a ventriculogram. Many patients with brain tumors show certain neurologic features which localize the growth to some extent, such as slight weakness or sensory changes on one side of the body, homonymous visual field defects, or possibly cerebellar signs which are not conclusive. In these patients a good-sized exploration over the suspected region might disclose the tumor in a fair number of instances, but by the injection of air into the ventricles the exact area for the craniotomy can be ascertained and the operation, therefore, undertaken with assurance. In modern neurosurgery a negative exploration should almost never occur.

lumbar puncture. In general, ventriculograms are preferred when there is evidence of increased intracranial pressure, whereas encephalography is used in conditions in which such pressure is not present.

#### USES OF VENTRICULOGRAPHY

The 106 ventriculograms were carried out largely on patients in whom a brain tumor or brain abscess was suspected. In 72 instances a tumor\* was disclosed and in 3 the patients had abscesses. The remaining 31 patients had conditions such as increased intracranial pressure without tumor (arachnoiditis or encephalitis), cerebral vascular disease, intracerebral hemorrhage, and other infrequent lesions.

For the most part, ventriculography was performed in order to get information on the following three points:

1. *To Diagnose the Presence or Absence of a Brain Tumor in Patients Having Choked Disks and Other Pressure Symptoms But No Localizing Signs.*—Cases 1 and 2 are examples of the first point.

CASE 1.—E. La P., a 41-year-old woman, was admitted to the New England Deaconess Hospital on Aug. 30, 1944. At the time of admission she was entirely disoriented and uncooperative. Her chief complaint was "frontal headache" for an indefinite period, and her husband stated that during the past year she had become listless, neglectful of herself and her home, and her memory had become poor.

Neurologic examination showed memory loss and disorientation as noted, together with some drowsiness and inattention. There was slight weakness of the lower left side of the face, but otherwise the cranial nerves were normal, although the fundi showed some early edematous changes. She had slight questionable weakness of the left arm and leg and the deep reflexes were greater on the left. A lumbar puncture done elsewhere revealed a pressure of 260 mm. The chemical examination of the fluid was normal in all respects. Roentgenograms of the skull showed some displacement of the pineal shadow downward and to the left according to one examiner, but this could not be confirmed by measurement.

A ventriculogram was carried out on Sept. 6, 1944. This showed the third ventricle displaced to the left, while the right lateral ventricle was displaced upward and outward. On the same day a right frontal craniotomy was performed and a deep, subcortical astrocytoma was subtotally removed from the medial portion of the frontal lobe and from the lateral ventricle.

Although the patient went through the operation in good condition she succumbed the following day to sudden respiratory failure. Necropsy revealed a chronic mitral and tricuspid endocarditis.

*Comment.*—While a frontal lobe tumor might have been suspected in this woman, such a localization without air would have been entirely guesswork and even if the correct area had been explored, the tumor might never have been found.

One patient (Case 2) had pressure symptoms and signs with no localizing evidence, and without air studies it was impossible to tell whether or not a tumor was present.

\*During the year in question there were 126 brain tumors verified histologically by operation. In 81 instances one or the other form of air study was used previous to operation (ventriculograms 72; encephalograms 9). Air studies, therefore, were felt to be necessary in 64.2 per cent of subsequently verified intracranial growths. If one excludes 16 pituitary adenomas and 4 acoustic neuromas since they can almost always be diagnosed without air, the figure rises to 76 per cent.

dilated lateral and third ventricles left no doubt as to the tumor's location. In some patients with similar findings the growth might be located in the third ventricle or even in one of the frontal lobes, so that when there is any doubt at all an air study should always be instituted.

A good illustration of the use of ventriculographic evidence in the presence of what turned out to be false localizing signs is shown by Case 6.

CASE 6.—H. F. F., a 38-year-old woman, was admitted to the New England Deaconess Hospital on Aug. 17, 1944. She had a history of acute headaches and projectile vomiting, coming on some three weeks before admission. She had likewise had occasional dizziness and blurring of vision.

Neurologic examination disclosed slow nystagmus to the right and left and early choked disks of 1 to 2 diopters. The other cranial nerves were negative. Gait was somewhat unsteady and she swayed in the Romberg position but did not fall. Finger-to-nose tests showed slight ataxia, especially with the left hand. The deep reflexes were rather inactive and equal throughout.

On Aug. 21, 1944, a ventriculogram showed the lateral and third ventricles displaced to the left, and the right lateral ventricle was depressed in its posterior portion. A right parietal craniotomy was performed on the same day and a partly cystic but largely solid fibrillary astrocytoma was subtotally removed. The patient was discharged improved on Sept. 2, 1944.

*Comment.*—There is little doubt but that this patient would have had a cerebellar exploration if localization had been based solely on the neurologic findings, and of course no tumor would have been found. Ventriculography, therefore, was the only means of locating the growth.

#### USES OF ENCEPHALOGRAPHY

In patients who have no clinical evidence of increased intracranial pressure and in whom a brain tumor is not suspected we have used injections of air by the lumbar route for a wide variety of purposes. Occasionally an unsuspected intracranial new growth will be brought to light, and this was true in 9 instances among the 323 encephalograms performed during the period indicated. Perhaps one of the greatest diagnostic functions of encephalography is to distinguish between cerebral vascular disease and a possible tumor. Before the advent of air injections this problem arose in a large number of patients who were seen particularly on the medical wards in consultation. In a high percentage of individuals who came to necropsy a tumor was disclosed when the clinical diagnosis had been vascular disease. This error should almost never be made at the present time when the means of making a correct diagnosis are available by air insufflation.

Detailed case reports to illustrate all of the increasing uses of encephalograms are unnecessary. The following list comprises the majority of the problems for which we have used this form of air study:

1. To distinguish cerebral vascular and degenerative disease from tumor.
2. To demonstrate the presence or absence of a localized lesion in epilepsy.\*

\*Occasionally even in patients who have focal seizures air studies may appear normal in the presence of a brain tumor as shown by Poppen and Peacher,<sup>2</sup> but exploration in such cases is almost always indicated sooner or later.

3. To demonstrate the existence of an obstructive or a communicating hydrocephalus in children.

4. To demonstrate the presence or absence of a possible cerebellar or high cervical lesion (such as Arnold-Chiari syndrome) in patients in whom multiple sclerosis or cerebrospinal degenerative disease is the probable diagnosis.

5. To be sure that no possible intracranial surgical lesion exists in certain cases of presumed cerebral birth injury.

6. To use as a therapeutic measure in post-traumatic headache.

This latter function of encephalography deserves special mention. It was first utilized for this particular type of headache by Penfield<sup>4</sup> who, in 1927, reported on seven patients who had been relieved by this means. Penfield emphasized the importance of filling the subarachnoid spaces completely irrespective of whether the ventricles were filled. During the year which forms the basis for this report we utilized lumbar air insufflations on twenty-two patients as a therapeutic measure for headaches following trauma. At the moment, figures are not available as to the percentage of cures effected, but it is my strong impression that roughly three out of every four patients were relieved. It is certainly a most valuable aid in the treatment of this type of syndrome which seldom can be alleviated by any other means.

#### SUMMARY

The introduction of intracranial investigation by the injection of air into the cerebral ventricles and subarachnoid spaces was an epoch-making advance in neurologic diagnosis.

Examples of the value and extent of such studies in a neurosurgical clinic during the course of one year are summarized.

The employment of air injections has made possible the diagnosis and operable approach to a vast number of intracranial lesions which would otherwise have remained undisclosed and therefore inoperable.

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# THE INNERVATION OF THE VEINS

## ITS ROLE IN PAIN, VENOSPASM, AND COLLATERAL CIRCULATION

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RECENT investigations have shown that the nerves of veins, arteries, and lymphatic vessels involved in cancer are responsible for much of the pain.<sup>1</sup> For this reason a knowledge of the vascular innervation is a prerequisite for the treatment of pain in cancer by means of sympathetic operations. A review of the literature shows that the anatomic and physiologic studies to date have been chiefly concerned with the sympathetic innervation of the arteries, but the lymphatic vessels are intimately related to the wall of the blood vessels, and the sympathetic nerves of the veins are affected by the cancer.

In phlebitis and thrombophlebitis the investigations of Leriche and Kuntz,<sup>2,3</sup> and Ochsner and DeBakey<sup>4</sup> have demonstrated that the sympathetic venous innervation plays an important role in the pain and in the vasomotor disturbances that accompany this disease. This shows the importance of determining the role of the innervation of the veins in pain, venospasm, and collateral circulation.

### ANATOMICO-PHYSIOLOGIC FACTS CONCERNING THE INNERVATION OF THE VEINS

The few data available suggest, as Kuntz<sup>5</sup> has said, that the general plan of the distribution of the nerve components observed in the arteries obtains likewise in the veins. On the other hand, it is now admitted that the nerve supply to the blood vessels, and among them the veins, in addition to the efferent vasomotor components contains also afferent sensory pathways. The afferent fibers are components of the sensory cerebrospinal nerve roots but the extent of the distribution of such fibers and their relationship to other nerve components are not definitely known.

The large veins of the thorax and abdomen are supplied with nerve fibers that arise in the autonomic nerves located near them. The proximal segment of the large veins of the limbs near the sympathetic chain receives its nerve supply from the sympathetic ganglia and trunks located near them. But the peripheral vessels are supplied by sympathetic fibers which join them via the somatic nerves lying close to them (Kuntz<sup>5</sup> and Hirsch<sup>6</sup>). The sympathetic fibers running along the somatic nerves are distributed to the peripheral vessels at irregular intervals (Potts<sup>7</sup>).

From patients in whom periarterial sympathectomy has been performed, some observations led a number of authors to a different conception of the innervation of the vessels. It is their belief that long nerve fibers probably arise in the aortic plexus and its branches or in the sympathetic chain and, passing along the adventitia of the peripheral arteries, play an important role in the innervation of the proximal and peripheral parts of these blood

showed the saphenous vein permeable all the length of the leg in the region where the clinical signs of phlebitis were evident. The pain disappeared after the novocain injection and the relief was maintained for a period of two hours. After this period the pain returned but it was not so intense as before; it was then completely relieved by a sympathetic block at the level of the third lumbar sympathetic ganglion. In this case the intravenous injection of novocain relieved the pain temporarily and at the same time relieved the spasm of the saphenous vein (Fig. 1).

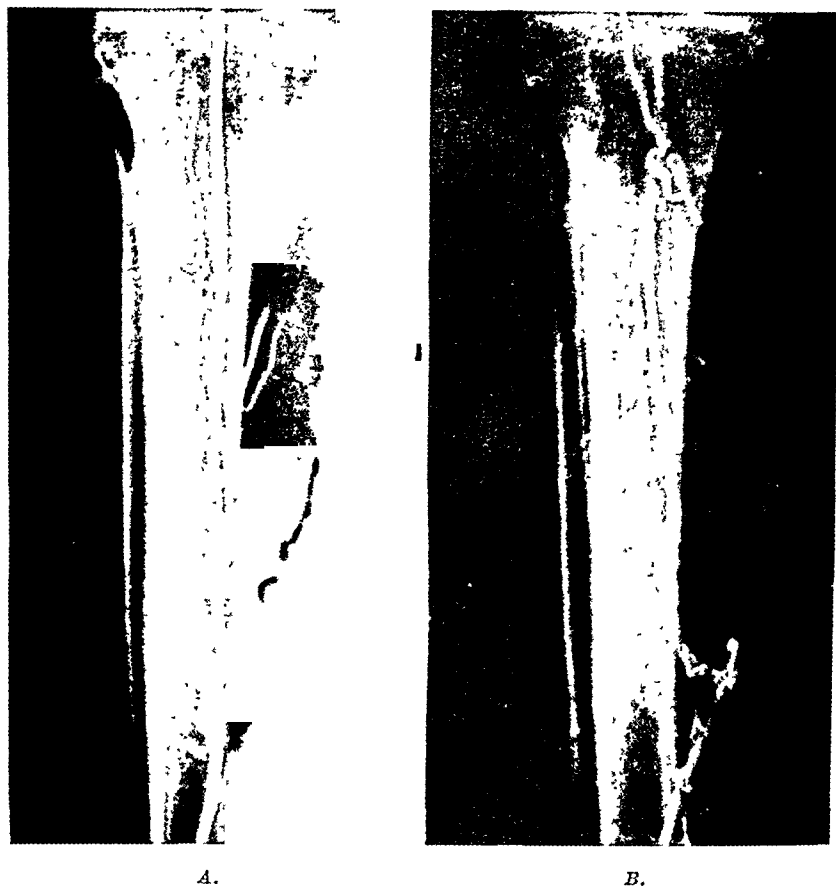


Fig. 1.—Acute phlebitis of the right internal saphenous vein in B.S.C., 60 years old. Venographies performed before (A), and forty-five minutes after the intravenous anesthesia (B), obtained by the injection of 15 c.c. of 1 per cent procaine hydrochloride into the lower extremity of the internal saphenous vein. In the second venography the venospasm shown at 1 in A disappeared and the saphenous vein is visualized in all its length through the leg (2) in B.

In a second patient with acute thrombophlebitis of the right saphenous vein; also studied by the venographic method, the saphenous vein was impermeable in all its length through the leg. With 30 c.c. of novocain (1 per cent) I blocked the third lumbar sympathetic ganglion of the right side, and two hours later a second venographic study was made under exactly the same technical conditions as the first. Twelve minutes after the sympathetic block the spontaneous pain had disappeared and the relief was maintained for a period of twenty-four hours. Then a slight painful sensation reappeared in the upper

segment of the saphenous vein; this was entirely relieved by a second anesthetic block of the sympathetic chain. Two hours after the first sympathetic block the patient was free from pain and the venographic study showed that the venospasm had disappeared and that the saphenous vein was permeable in the lower two-thirds of the leg. The upper third of the vein was obliterated. In this case there was also an increase in the development of the venous collateral circulation. The study of this case shows that the pain and the venospasm were relieved by the anesthetic block of the lumbar sympathetic chain. Moreover, the vasodilatation of the saphenous vein persisted after the anesthetic block of the sympathetic chain (Fig. 2).



Fig. 2.—Acute thrombophlebitis of the superior third of the internal saphenous vein of the right leg in J.A., 44 years old. Venography was performed before and two hours after the anesthetic block of the lumbar sympathetic chain. In the second venography it will be observed that the venospasm (1,A) has disappeared and the saphenous vein is permeable in the lower two-thirds of the leg (2,B). There is also an increase in the collateral venous circulation.

The results in the first patient show that anesthetization of the nerve endings in the venous wall by the intravenous injection caused the disappearance of the venospasm and relieved the pain in the vein. In the second patient interruption of the sympathetic pathways of the saphenous vein by anesthetizing the lumbar



chain was followed by relief of pain, more immediate and of longer duration. The venospasm also disappeared and the vasodilatation with increase in collateral circulation two hours after the sympathetic block persisted. These investigations demonstrate that the anesthesia of the nerve endings in the venous wall or of the afferent and efferent pathways in the lumbar sympathetic chain relieve pain and venospasm. And since the venous vasodilatation and the relief from pain lasted for a longer period than the action of the anesthetic, it seems logical to conclude that in these cases venospasm played a role in the mechanism of pain arising in the veins.

The pathway of pain fibers arising in the veins is indicated by the relief obtained by blocking the sympathetic chain: the afferent sensory fibers conducting painful impulses from the wall of the veins traverse the sympathetic chain to reach the spinal cord. That sensory fibers may pass through the sympathetic chain to join the somatic rami of the spinal nerves was claimed by Förster,<sup>15</sup> Kuntz and Farnsworth,<sup>16</sup> and others, but Burget and Livingston,<sup>17</sup> and Moore and Singleton<sup>18</sup> did not agree with this. My investigations show that interruption of the sympathetic chain relieves the pain in phlebitis and thrombophlebitis.

#### SYMPATHETIC INNERVATION OF THE VEINS AND VENOSPASM

A number of observations support the view that the veins are innervated by vasomotor efferent fibers that control their tonus. De Takats,<sup>19</sup> discussing the role of venospasm in thrombophlebitis, frequently found a firm, hard cord, palpable in the groin during the first few hours of thrombophlebitis: this disappears under heat and elevation. He also referred to the contraction of the cubital vein induced by a traumatizing venous puncture, and the presence of spasm of the adjoining venous segments in patients with varicose veins treated by injection. I have also observed several times a venous spasm following the mechanical or chemical stimulation of the innervation of the wall of the femoral, saphenous, and cubital veins. It is interesting that the intensity of the venospasm induced by stimulating the adventitia of the veins varies in different individuals.

In 1938, Leriche,<sup>3</sup> suggested that phlebitis is dominated in its symptomatology and evolution by three factors: venospasm, the extension of coagulation, and that of the arteriospasm. The venospasm that he regarded as constant, and also as being the cause of pain, favored the extension of blood coagulation by decreasing the velocity of the blood circulation. Thus, an obliterated vein is not only functionally suppressed but it behaves in an abnormal manner through stimulation of the nerves in the adventitia. Leriche believed an obliterated vein behaves exactly like an obliterated artery. A thrombosed vein originates vasoconstrictor reflexes in contiguous veins and arteries. Ochsner and his co-workers<sup>20</sup> have demonstrated experimentally that localized chemical endophlebitis results in marked arteriolar vasospasm. They found the mechanism in these cases to be the result of sympathetic vasoconstrictor impulses that began in the involved venous segment. Ochsner concluded that these

reflexes are transmitted over the sympathetic system since sympathectomy or anesthetic sympathetic block prevents these reflexes.

The investigations of Reichert<sup>21</sup> and Homans<sup>22</sup> indicate that in thrombophlebitis the venous obstruction is insufficient to produce the degree of edema that results from perivenous lymphatic obstruction. Zimmermann and De Takats,<sup>23</sup> however, concluded that the venous obstruction is the most important factor and that lymphatic obstruction plays a minor role in the mechanism of thrombophlebitic edema. From many experiments on the veins and lymphatics of dogs, Fontaine and I<sup>24</sup> have demonstrated that mechanical venous and lymphatic obstruction is of secondary importance. We have found that ligations, resections, or obliterations of the larger venous trunks and of their affluents, at the level of the root of a limb, cause only a transitory edema. We have observed also that when the lymphatics are obliterated by sclerosis in addition to the venous obstructions, the postoperative edema is of longer duration. Since the edema disappears completely in these experiments we are led to conclude, with Leriche, that neither the venous mechanical factor nor the lymphatic factor is enough to explain wholly the phlebitic edema. These facts and others that I have observed in clinical cases of phlebitis lead me to accept the view held by Leriche, Ochsner, and DeBakey that the innervation of the veins plays the most important role in the symptomatology and therapeutics of phlebitis.

In order to investigate the effects of venospasm, Papper and Imler,<sup>25</sup> made phlebographic studies of the veins of the lower extremity before and after anesthetic block of the lumbar sympathetic chain in three patients, the first with clinical chronic cellulitis of the right leg, the second with thromboangiitis obliterans, and the third with chronic recurrent migratory phlebitis of the right great saphenous vein. They confirmed the diagnosis of venospasm in these cases by blocking the lumbar sympathetics; following this the venous deformity produced by the narrowing of the spasmodic vein was abolished.

The investigations carried out by Dougherty and Homans<sup>26</sup> and Dos Santos<sup>27</sup> on the roentgenographic visualization of the venous system provided an interesting method of studying the role of the vasomotor innervation of the veins. In patients with acute phlebitis or with thrombophlebitis of the lower extremities, I have studied by this method the effects of interrupting the efferent vasomotor fibers on venospasm of the saphenous vein.

The existence of venospasm associated with acute phlebitis or with thrombophlebitis is clearly demonstrated in the two cases already mentioned. In the first patient, who had acute phlebitis of the right saphenous vein, there were clinical signs of phlebitis in all the length of this vein at the level of the leg. The venographic study showed that this vein presented a diminished caliber in the middle third and was completely impermeable in the upper third of the leg (Fig. 1). Forty-five minutes after the injection of 15 c.c. of novocain at 1 per cent into the lower part of the saphenous vein, the spasm had completely disappeared and the venographic study showed that it was uniformly patent throughout. The second patient had an acute thrombophlebitis of the right saphenous vein in the upper third of the leg. The venographic study

(Fig. 2) showed the vein to be totally occluded. Two hours after the third right sympathetic ganglion had been blocked with procaine hydrochloride, the venospasm had disappeared and the saphenous vein showed obliteration only in the upper third and permeability in the lower two-thirds of the leg. These cases demonstrate clearly that acute phlebitis or thrombophlebitis may be accompanied by venospasm and that this venospasm may be relieved by intravenous anesthesia of the inflamed vein or by the anesthetic blocking of the efferent vasomotor pathways in the sympathetic chain.

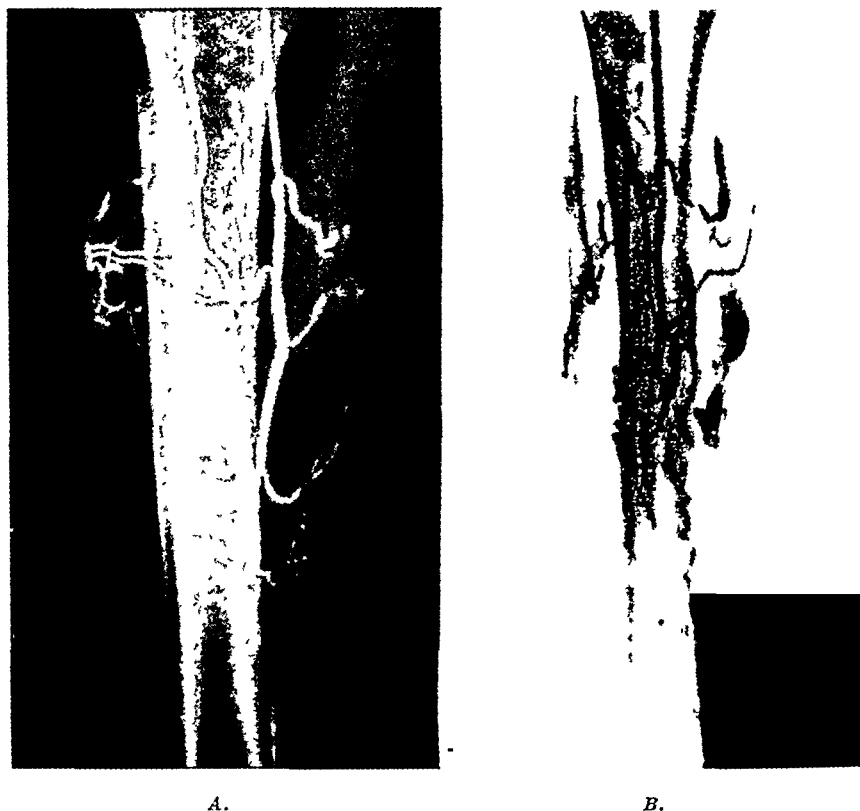


Fig. 3.—Thrombophlebitis of the deep veins of the right leg in A.L.C., 22 years old. Venography performed before (A) and one month later (B), after the treatment by eight anesthetic blocks of the sympathetic lumbar chain, (second, third, and fourth lumbar nerves). Following this treatment, pain and the edema disappeared and the later venography showed an increase in the development of the collateral venous circulation.

#### SYMPATHETIC INNERVATION OF THE VEINS AND COLLATERAL VENOUS CIRCULATION

Since the facts cited demonstrate the existence of a sympathetic efferent vasomotor innervation in the veins, it is important to know what part these nerves have to play in the development of collateral venous circulation.

Experimental and clinical investigations conducted by several authors (Leriche,<sup>3</sup> Linton and White,<sup>28</sup> Theis,<sup>29</sup> and others) have shown that interruption by sympathectomy of the vasomotor nerves of arteries increases the development of the arterial collateral circulation. My co-workers and I<sup>30</sup> have also verified these findings by experimental investigations on animals and have ar-

rived at the conclusion that the greater effect is obtained by section or by blocking the sympathetic ganglionic chain. But this conclusion is also exact so far as concerns the influence of the vasomotor sympathetic innervation on the development of the collateral circulation of the lymphatic vessels. We<sup>11</sup> have observed that if on dogs the femoral lymphatic vessels are interrupted by ligatures, anesthetic block or resection of the lumbar sympathetic chain increases the development of the collateral circulation of the lymphatic vessels.

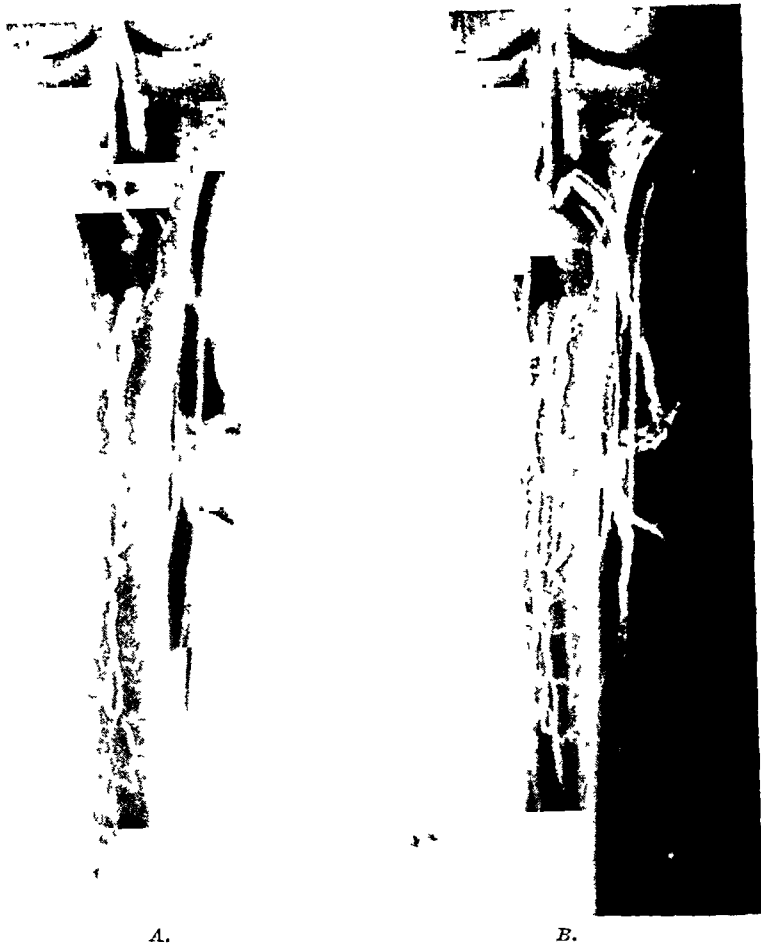


Fig. 4.—Thrombophlebitis of the deep veins of left leg in A C, 32 years old. Venography performed before (A) and one month after the perivenous sympathectomy of the femoral and saphenous veins (B). In the second venography (B) there is marked increase in collateral venous circulation.

Does the efferent vasomotor innervation of the veins exert a similar influence on the development of the collateral venous circulation? In approaching this problem I employed three different methods of interrupting the venous sympathetic innervation in patients with phlebitis or thrombophlebitis of the lower limbs.

*Series 1.*—In four patients, two with acute phlebitis and two with thrombophlebitis of the lower limbs, repeated anesthetic blocks of the lumbar sympathetic chain (second, third, and fourth lumbar nerves) were performed. In these

cases the number of anesthetic blocks varied between four and thirteen; they were made over a period of ten to thirty days. Venographic studies with uroselectan were made before and at the end of the treatment. They showed that the repeated anesthetic blocks of the lumbar sympathetic chain not only relieved the pain and modified the vasomotor disturbances but the collateral circulation of the veins was increased (Fig. 3).



Fig. 5.—Thrombophlebitis of the deep veins of the left leg in E.C., 47 years old. Venography performed before (A) and one month after the left lumbar sympathectomy (third and fourth lumbar nerves) (B). In the second venography (B) there is an increase in the collateral venous circulation in the lower third of the leg.

*Series 2.*—In two patients with thrombophlebitis of the veins of the legs, perivenous sympathectomy of the femoral vein was performed. Below the crural arcade the femoral vein was approached and the perivenous innervation was interrupted for a length of two inches. The innervation was also interrupted in the terminus of the saphenous vein. The operation was followed by relief from pain and amelioration of the vasomotor disturbances. The veins of the legs in these two patients were studied before and one month after the operation; visualization by x-rays showed a definite increase in the collateral venous circulation (Fig. 4).

*Series 3.*—Finally, in two patients with thrombophlebitis of the veins of the lower limbs the lumbar sympathetic chain was interrupted, the third and fourth sympathetic ganglia and the intermediate trunk being resected. A manifest improvement followed the operation in each case. Venographic studies one month later showed in each a definite increase in the venous collateral circulation (Fig. 5).

In these three series of patients with phlebitis or thrombophlebitis, interruption of the efferent vasomotor innervation of the veins of the lower extremities by repeated anesthetic blocks of the lumbar sympathetic chain, perivenous sympathetomy, or lumbar ganglionic (third and fourth lumbar nerves) sympathetomy was followed by an evident increase in the venous collateral circulation.

#### SUMMARY AND CONCLUSIONS

1. The veins are innervated by afferent sensory and efferent vasomotor pathways. Direct mechanical or chemical stimulation of the afferent pathways at the level of the wall of the veins may cause pain. The relief of venous pain and venospasm in acute phlebitis and thrombophlebitis by intravenous anesthesia of the inflamed vein or by the anesthetic block of the sympathetic chain, for a period longer than the anesthetic action of the drug employed, suggests that venospasm may play an important role in the mechanism of pain.

2. The observations in these cases demonstrate also that acute phlebitis or thrombophlebitis may be accompanied by venospasm extending far beyond the phlebitic or thrombosed vein. This venospasm may be relieved by peripheral anesthesia of the venous wall or by interruption of the efferent pathways of the sympathetic chain.

3. In cases of thrombophlebitis it was observed that repeated anesthetic blocks of the sympathetic chain with procaine hydrochloride, perivenous sympathetomy, or resection of the regional sympathetic chain was followed by an increase in the collateral venous circulation.

4. These investigations have demonstrated that physiologic or anatomic interruption of the innervation of the veins may relieve the pain and the venospasm, and it also increases the development of collateral circulation.

5. The facts observed suggest that the plan of the innervation of the veins in relation to pain, spasm and collateral circulation is similar to that of the afferent sensory and the efferent vasomotor pathways of the arteries.

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## THE PRACTICE OF SURGERY IN JAPANESE PRISON CAMP HOSPITALS IN BURMA AND SIAM

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**I**N THIS paper an attempt will be made to record briefly the diagnostic and therapeutic methods adopted by the surgical staff in the primitive so-called hospitals of the Japanese Prison Camps in 1942-1945.

I was the senior medical officer and surgeon in charge of 1,800 United Kingdom, Australian, Dutch, and American prisoner of war patients at Kohn Kuhn, an abandoned working camp, Burma, in 1943, and chief medical officer and consulting surgeon at the prisoner of war hospital camp of 8,000 patients at Nakampaton, Siam, in 1944-1945. The Japanese medical officer confined his activities to discharging men for work. The Burma-Siam Railway was under construction and the Japanese were forcing the pace. Every prisoner who could work or even walk was compelled to do his utmost. The diet was meager—rice in sufficient quantities and polished, but meat supplied in amounts varying from 1 to 2 ounces per man per day. Vegetables were of the cucumber-radish-spinach variety. Protein deficiency was marked.

*Pellagra.*—Pellagra was responsible for many deaths.

Patients were admitted to the jungle camp hospital in all stages of debility. Sore mouth, fissured tongue, sore pharynx, anorexia, and diarrhea were common. Skin rashes of the pellagrous type were seen in a few. Mental changes occurred in a small number. Post-mortem examination revealed in all the shrunken organs, spleen, liver, and heart, and a "diaphanous" bowel, a small, thin-walled stomach and intestine, so-called "rabbit gut," and in some a shrunken brain with secondary hydrocephalus and convolutional atrophy.

Malaria was universal and quinine, the only drug supplied by the Japanese, was provided for 300 patients, that is, those patients admitted with malaria as the primary disease. One disease was permitted by the Japanese Medical Service, hence the patients with pellagra, dysentery, and tropical ulcer were "not allowed to have malaria" by order of the Japanese.

No treatment was available for the patients with pellagra. Food was insufficient and nicotinic acid, even if available, would not have cured them, as the changes in many were obviously irreversible.

Dysentery was not the scourge it was in some camps. Hygiene was reasonably good. A hut of 100 was labeled "the death house" and to it were taken patients with infectious diseases (bacillary and amebic). Some died following perforation of the colon; others developed masses, especially in the right iliac fossa; and still others sloughed great casts of the colon and rectum before they died. My death reports, which the Japanese always insisted should be written in detail, were condemned by the Japanese doctor at headquarters because I used the term amebic dysentery. It was forbidden; the word diarrhea had to be substituted. After protests and much correspondence, followed by á



visit from a Japanese Lieutenant Colonel, it was admitted that a clinical diagnosis of amebic dysentery in the absence of microscopic findings would be accepted and apologies were offered that there was no Japanese supply of emetine. A colleague procured for me in another Japanese camp, a bottle of ipecacuanha extract from which a Dutch officer, who acted as one of my medical orderlies, extracted 150 1 gr. doses of emetine. A short course of five injections of this homemade alkaloid was given to fifty patients with wonderful results.

I, personally, having suffered from amebic dysentery can speak feelingly of the dramatic effect of emetine. Many of the patients had ulcers in the rectum, and a proctoscope made from tin was constructed which enabled me to obtain a good view of the whole rectum when the patient was placed in the knee-elbow position. Sunlight reflected by a mirror illuminated the interior of the rectum and much information concerning the progress of the lesions was gained from regular rectal inspections. Ulceration and necrosis of the "valves" was common and in some was followed by stricture. Dilatation by bamboo dilators was practiced and succeeded in most; colostomy was required in one patient because of obstruction. This patient was later, at Nakompaton, subjected to a Kraske type of resection of the local fibrosed rectum with excellent results.

*Ulcer.*—Ulcer of the leg and occasionally of the hand, arm, and body occurred in great numbers. In that camp 500 cases were classified as tropical ulcer. At least sixty patients had ulcers on both legs, some had two or more ulcers on one leg. The term tropical ulcer was used for this condition, but as my Dutch colleague pointed out, the ulcers did not conform to the type commonly seen in the tropics and known by that name.

Until May, 1943, I had treated some hundreds of ulcers of the leg in prisoners of war in Sumatra and Burma. They were the usual circular ulcer from 1 to 5 cm. in width, circular, having a sloughing base on the fascia.

Foments, curettage, and iodoform and bandaging for several days were usually sufficient to bring about healing. There were many in the 500 previously mentioned which were of the usual type, but many followed a more malignant course. Spreading peripherally, eroding the fascia, periosteum, and even blood vessels, they enveloped the leg, leaving muscle and bone exposed. Black necrotic areas of fascias and tendons were excised. An attack of malaria or an exacerbation of pellagrous diarrhea was accompanied by a rapid spread of the ulcer. The usual methods of curettage, foments, etc., failed. Iodoform was not available. Where the process involved tendons and muscle, radical excision of those structures was carried out—even the tendo achillis were excised in a number of patients, the tibialis anterior, posterior, and the peroneal tendons were often cut out. Altogether sixty patients were treated in that fashion. Many recovered, the leg was saved, and surprisingly little loss of function resulted. Despite these measures, and all attempts at conservatism, the process in many spread up the periosteum of the tibia, opened the ankle joint, or caused such widespread gangrene of muscles that amputation was done. The mid-thigh

amputation was performed in most; twenty-five amputations were done below the knee.

Fortunately, I had a bottle of cocaine tablets in my possession and as no general anesthetic or novocain was available I experimented with spinal cocaine. One and one-half cubic centimeters of a 2 per cent solution sufficed to produce anesthesia to the groin and in most cases did not paralyze, so that the patient cooperated with the surgeons in the operation.

In that camp 120 legs were removed. All patients survived operations but many died months later of pellagra, malaria, or dysentery. The survivors number 50 per cent but they slowly made progress and are among the most grateful patients one could ever have.

Many problems confronted us in the camp. No facilities for operating were provided or, indeed, allowed. The abandoned bamboo huts of the former working camp provided the accommodation and a small annexe to a hut, open to the four winds of heaven on three sides, was the operating theater. A bamboo table was set up; towels and odds and ends of clothing were boiled up as dressings. No antiseptics were available, but we overcame this difficulty by using homemade rice alcohol. This was prepared in 90 per cent strength from the scraps of rice thrown away by the pellagrous patients. There was plenty of it. A small quantity of soap was obtained from the Japanese and this was supplemented by soap made locally from scraps of fat and ashes.

Catgut was necessary as I was afraid to use nonabsorbable ligatures for the femoral artery, in the presence of so much sepsis. Cotton was used for skin suture.

The catgut was prepared under my instructions from the peritoneum of the small intestine of the local ox, killed for food (the submucous coat proved too fragile). Strips of peritoneum were twisted on a stick and my medical orderlies became expert at it. Sterilization of the catgut was done by placing it in a tin in the rice oven, after the fires were raked out. After this was repeated for sport killing the gut was stored in the alcohol mentioned previously.

A reliable ligature was thus made which was used not only for arteries but also for suturing the abdominal wall in a few patients who came to immediate operation. A better method of sterilizing gut was later devised, that is, suspending a tin of the wound gut in another tin of boiling saturated salt water for one hour at a time.

A few cases of secondary hemorrhage occurred at the stump and in view of this risk, in patients being transported to Siam when the camp was clearing, I ligatured the femoral artery in Scarpa's Triangle as well. Amputation was circular with short flaps sutured anteroposteriorly in some—in others, loosely held together by one or two sutures because of sepsis.

The absence of pus formation was an outstanding feature in the cases mentioned. Toward the end of 1943 I organized an underground supply of meat to the sick, paying recovered patients of the more daring type to bring in cattle from the neighboring villages to the precincts of the camp and killing

at night. This was done in defiance of the Japs and under the nose of the guards. The effect of the extra meat was soon obvious: large ulcers began to suppurate, exposed bone became a sequestrum, and the limb was saved. Some of these patients were later operated on, the sequestrum in some cases being three-quarters the length of the tibia and the complete anterior half of the tibia being successfully removed. A single one sustained a fracture in the remaining involucrum, but union occurred in time.

In my daily visits to these patients with severe ulcers (I could see only seventy or eighty in a morning) how I welcomed a little pus and how encouraged the patient was when the dreadful pains of necrosis and ischemia gave way to inflammation with its local sequelae.

No microscopic examination of the discharge, which was usually thin and watery, was possible. In a few cases the muscles in the amputated limb were brick red in color suggesting an anerobe, but there was only one case of fulminating infection simulating gas gangrene and that in a medical orderly in the ulcer hut, who scratched the back of his hand on the bamboo bed of a patient with ulcer. Amputation of the right arm was necessary. The usual history was of a scratch by bamboo or stone, the abrasion failing to heal and spreading as an ulcer. The edges were necrotic with a tendency to undermining. The base was a slough, sometimes black and adherent, at other times soft and exuberant.

*Nutritional Edema.*—Nutritional edema was common, often called beriberi, especially for the records of the Japanese who actually understood that term.

Ascites, pleural effusions, edema, of limbs, and finally fatal edema of lungs and glottis occurred in some. Should the patient survive the edematous stage the fluid usually drained away and he died an emaciated skeleton. Meat and restricted fluids were the treatment, but only in the later stages at this camp was this feasible, and then many were past help.

Limbless men were provided with a light bamboo pylon and crutches (camp made). About 300 patients died in this camp in six months. The residual sick, together with similar patients from camps elsewhere along the railway, were transported by train to a newly constructed sick depot at Nakompaton, 45 kilometers from Bangkok.

#### SUMMARY

As chief medical officer and consulting surgeon at this "hospital" which accommodated 8,000 sick prisoners of war at one time I continued to work from January, 1944, to August, 1945. The majority of the cases were medical, for example, 1,500 chronic dysentery (mostly amebic), 1,100 avitaminosis, 1,200 surgical, the remainder skin, permanent disabilities such as amputations, and convalescents. The conditions in this camp were better than anything we had experienced in the jungle, but were far below the standards of most primitive European hospitals. There were no beds or bedding, and no specific drugs except quinine. Improvisation of instruments and operating equipment continued on a large scale, but the arrival of American Red Cross stores including some emetine and the sulfa drugs in July, 1944, relieved the situation. This

supply formed the basis of our dispensary stock; surgical instruments so supplied were retained by the Japanese. Operating was done with naked hands, scrubbing up in dishes with soap, and then immersion in camp-made 90 per cent alcohol. British, Dutch, and Australian surgeons worked as a team. A concrete floor and fly wire were provided in a special hut for the operating theater. Great attention was paid to detail of hemostasis and antisepsis (each layer in a hernia or appendix operation was painted with alcohol before closing). In 120 patients with herniotomy only two developed a mild sepsis. The soldering iron was used as cautery in mouth, neck, rectal, and pelvic operations. Silver clips made from beaten forks and fine cotton were freely used as hemostats. Homemade catgut was used for abdominal suture and ligature of large vessels. Nearly 1,000 major operations were performed. Patients with peptic ulcer were regularly "milked" for acid which was used for patients suffering from hypochlorhydria.

Spinal anesthesia\* and local anesthesia were employed almost exclusively.

Fifteen hundred transfusions of defibrinated blood were given to debilitated and anemic patients. Cross typing was carried out in the usual way.

Sequestrectomy and skin grafting of old ulcers was done extensively.

Patients with chronic colon infection despaired of by the physicians were submitted to ileostomy. Physiotherapy and rehabilitation were important activities in 1944-1945. One hundred seventy-eight limbless men were fitted with camp-made wooden artificial limbs.

Full details of the surgical work have been recorded in the Official War Diary of the camp, copies of which have been supplied to the medical directors of the respective nations.

Naturally, in the absence of x-ray and other diagnostic equipment, surgeons were forced to rely on the case history and the physical findings. The eyes, fingers, and other senses were exercised more freely. Such an enforced return to fundamental methods was not without compensation. Analyses of post-mortem results and discussions at "death" meetings had a salutary effect and indicated that diagnosis was not so frequently in error as might be imagined.

In March, 1945, the Japanese prohibited post-mortem examinations for obvious reasons.

The technical work in the surgical field was of a good standard and great credit is due to the surgeons, Lieutenant Colonel Dunlop (A.A.M.C.), Major Kranz (A.A.M.C.), Captain Maconachie (R.A.M.C.), Captain Winkel (D.A.M.C.); to Captain Marcowicz (R.A.M.C., blood transfusion officer and biochemist), Captain Cyril Vardy (R.A.M.C., my adjutant and registrar), Major T. Marsden (R.A.M.C., pathologist), Doctors Chapman and Kostermanns, scientists; and to my colleagues of the Triumvirate of Control, Lieutenant Colonel Malcolm (O.B.E., M.C., R.A.M.C.), and Lieutenant Colonel Larsen (D.A.M.C.), and to the many medical orderlies of four nationalities who contributed so much to the success of the surgical department of the Nakompton Prisoner of War Hospital.

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\*Cutcaine, American Red Cross.

## CEREBRAL FUNGUS FOLLOWING PENETRATING WOUNDS

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A REVIEW of 426 cases of penetrating wounds of the head personally studied in two neurosurgical centers revealed 32 instances of cerebral fungus. The incidence was thus 7.5 per cent. All of the patients were battle casualties, having been injured in the Mediterranean Theater of Operations during the period of November, 1942, to February, 1945. As in the vast majority of that 20 per cent of this particular series of brain wounds in which deep infections developed, the organisms were of relatively low virulence.<sup>1</sup>

Cerebral fungus is a subacute or chronic herniation of the brain through a defect in dura, skull, and scalp, accompanied by infection, deep or superficial, or both. In chronic infected hernias progressive organization of the extruded and superficial portions into scar tissue is usually evident. The exact time of transition from cerebral herniation (the acute phase) to that in which a fungus may be said to exist depends, in our definition, upon these tissue changes. Gross evidence of such processes characteristic of fungus has usually begun to appear at the end of seventy-two hours. Cerebral fungus formation is one of the more serious complications of any craniotomy, but it is by no means a hopeless or necessarily a fatal one.<sup>2-7</sup> It is regarded as the result of failure of wound healing in the presence of infection; thus, while the fungus per se may require excision, attention must be directed primarily toward the diagnosis and elimination of such underlying causative factors as cerebral abscess or hematoma.

While the severity of the infection, the extent of tissue loss or damage, the size of the bone-dura aperture, and the state of the fungus were different in each patient, study of their causes and characteristics permits classification into two fairly distinct groups. In the first are included those cases in which the cerebritis was only superficial; bone or shell fragments might or might not have been retained. Intracranial pressure was normal or but moderately elevated. These we have termed "benign" fungi. Into the second group fell those cases in which local cerebritis, similar to that mentioned, was associated with, and increased by, cerebral abscess, hematoma, or a mass of necrotic brain tissue. In patients with abscess formation, retained bone chips or metallic foreign bodies could usually be demonstrated roentgenographically. There was always an increase in the intracranial pressure which was often progressive, and the growth of the fungus was relatively rapid. This type we have called "malignant" fungus.

### BENIGN FUNGUS

Of this group of thirty-two patients with cerebral fungi, thirteen fell into the benign category. In each there was a superficial wound infection in the presence of an open dura mater. The protrusions grew slowly, they were not

shaggy nor sloughing, and they did not bleed easily. There were no symptoms suggestive of a high intracranial pressure, and neurologic evidence of extension of the process deep within the cerebrum was lacking. Retained bone chips were demonstrated in but four patients. These were removed at subsequent operation in three instances; neither abscess nor hematoma was found. The fourth patient was evacuated without operation because of the urgency of the military situation. A fifth individual was operated upon primarily for the excision of a fungus the size of a golf ball. This was found to be undergoing fibrosis and organization, and in retrospect it appeared likely that healing would have followed just as well had no operation been performed. Systemic but not local sulfonamide and/or penicillin therapy was practiced routinely in all cases. No patients were treated routinely by lumbar puncture; all hernias receded with eventual disappearance of the superficial infection, and with closure either spontaneously or surgically of the scalp defect. There were no deaths in this group.

A typical example of a benign fungus and its course is seen in Case 1.

CASE 1.—A soldier sustained a 4 cm. penetrating shell fragment wound of the vertex, to the left of the midline, in action in the Salerno landing, Sept. 9, 1943. There was a compound, comminuted, depressed fracture with a few indriven bone fragments. Right hemiparesis with motor aphasia was present. He was operated upon at an evacuation hospital twenty-four hours after injury, at which time scalp, bone, and cerebral portions of the wound were débrided with the removal of an estimated 7 Gm. of pulped brain. The dura was sutured, and the tripod incision of the scalp was closed without drainage. On Sept. 21, 1943, at a general hospital, the wound was noted to have become infected. By Sept. 25, 1943, a separation was present centrally with a small fungus presenting. A few small bone fragments were demonstrated by roentgenograms to be present in the extracerebral portion of the wound. Since there was no evidence of abscess or of sharply increased intracranial pressure, and since the hemiparesis was not increasing, no operation was undertaken. As the local infection cleared, the fungus receded and healing occurred satisfactorily. At no time while under observation was he critically ill, and he returned to the Zone of the Interior in good condition.

The forerunner of the fungus in this instance was the breakdown of the wound, superficial infection, and local cerebritis, together with a temporarily and moderately increased intracranial pressure. The latter slowly subsided with healing of the wound, thus making this fungus a self-limited complication.

Two patients entered the hospital six days after having been injured, Sept. 9, 1943, in the Salerno landing. Neither had been operated upon and the original dressings were still in place. Both patients had fungus formation, and the following brief record of one of them is illustrative of *this particular type*<sup>4</sup> of benign fungus:

CASE 2.—The patient was injured by shell fragments which guttered the left posterior parietal area, leaving a bone defect 2.5 by 3.5 cm. Many bone fragments were deeply indriven, and a few small metallic foreign bodies remained in the superficial layers of the brain. On arrival at the Head Center six days later there was a solid fungus filling the scalp defect, approximately 2.5 cm. in diameter. It was clean, firm, pulsating, and not hemorrhagic. There was no cerebrospinal fluid leak. A complete right homonymous hemianopsia was present. The patient was dull, passive, and aphasic to a marked degree in several spheres, but had no motor weakness. There was papilledema of 3 diopters. At operation on the same day the

scalp edges were excised, the bone edges freshened, and the tract débrided and cleansed of bone chips, hair, dirt, pulped brain, and a walnut-sized clot which extended down to the lateral ventricular wall. A solid scalp closure without drainage was effected. The patient made an uneventful recovery, having been left with moderate aphasia and right homonymous hemianopsia. He was sent to the Zone of the Interior shortly afterward with the wound well healed and the flap soft and pulsating.

This was a type of benign fungus occurring in an open wound which was not yet actively infected, but potentially so; there were retained bone chips and foreign bodies and an increase of intracranial tension due to the acute brain injury and clot rather than infection. Excision of the fungus, delayed but complete débridement,<sup>s</sup> and wound closure without drainage resulted in primary wound healing.

#### MALIGNANT FUNGUS

In this group are included those nineteen cases in which infected cerebral herniations, occurring subsequent to wound débridement, were associated with increased intracranial pressure caused by abscess, hematoma, or occasionally necrotic but uninfected brain tissue. Here the danger of meningitis and the complications of increased intracranial pressure were very real. Six of these patients died while under observation, and three others may have died later, since the military situation required their evacuation while critically ill.

The fungi, once started on their way through the open dura mater and bone, grew rapidly, as if propelled by the increased intracranial pressure behind them. As a rule they were shaggy, wet, and had a tendency to bleed. Signs and symptoms of increased intracranial tension were usually evident. While unfortunately the underlying nidus of infection, abscess, or clot can by no means always be located with exactitude by clinical signs, a roentgenologic demonstration of retained intracerebral foreign bodies or of bone chips offers a strong, although not invariably reliable, clue to its location. Gas or a foreign body which can be demonstrated to have shifted positions in serial roentgenograms clearly indicates a fluid-filled cavity. A purulent sinus may lead through the fungus, along a missile or bone chip tract, to the abscess and thus be a valuable guide at operation.

Until the infected mass is evacuated, be it a frank abscess or a deep cerebritis with or without hematoma, increasing tension will not be brought under control, nor the progress of the fungus arrested. Systemic chemotherapy with sulfonamides and/or penicillin was employed routinely, but served as an adjuvant to, rather than a substitute for, surgery. Operative removal of the causative factor is therefore urgently required in every case of malignant cerebral fungus. Delay or failure to find the associated abscess was responsible for the fatal outcomes in all of those patients who died. Meningitis may follow rupture of the abscess into the ventricle, the ventricle may rupture externally through the fungus, or death may result from the effects of increasing intracranial pressure.

Such a tragedy is illustrated by Case 3, in which the abscess, although sought for, was not found until too late.

CASE 3.—A 23-year-old engineer was struck in the left parietal region by a shell fragment on Oct. 13, 1943; a compound, comminuted, fracture resulted, with numerous indriven bone fragments. Right hemiparesis with partial aphasia followed. The wound was débrided eight hours later at an evacuation hospital and a foreign body and most of the bone fragments removed. Eight days later the patient arrived in North Africa. Purulent drainage from the wound was noted. The neck was somewhat rigid and the cerebrospinal fluid cell count was 8,700. Under sulfadiazine he was said to have improved gradually and was actually out of bed walking about until Nov. 19, 1943, thirty-seven days after injury. At that time severe headache and vomiting set in, the temperature rose to 103° F., and cervical rigidity reappeared. On admission to the Head Center on that date he complained of severe frontal headache. Incomplete nominal aphasia and right hemiparesis were evident. The neck was stiff and the temperature remained elevated. The cerebrospinal fluid cell count was 1,150, of which 850 were polymorphonuclear leucocytes. In the center of the left parietal wound there was a tense bulging fungus partially covered with granulation tissue. It was not pulsating. Some purulent drainage was evident. Roentgenographic examination disclosed a few, tiny, scattered bone chips beneath the defect and a metallic foreign body in the posterosuperior portion of the left temporal lobe. A diagnosis of brain abscess associated with incomplete débridement was made. The following day, under local anesthesia, the hernia was excised flush with the dura. Four sinus tracts were found and followed to their depths. Several bone fragments were evacuated, but no definite abscess, hematoma, nor mass of necrotic tissue was encountered, although one of the tracts extended approximately 7 cm. down into the temporal lobe. The hernia itself was quite necrotic and the walls of the sinus tracts were fibrotic. Cultures from the wound subsequently revealed anaerobic hemolytic streptococcus and aerobic nonhemolytic staphylococcus.

Although the brain was moderately slack at the close of this procedure, we were far from satisfied with the findings, or lack of them. Despite the fact that the spinal fluid pressure remained elevated (280 to 300 mm. water) one was lulled into a false sense of security by the improvement in the patient's general condition and the lessening of signs of meningeal irritation. Actually, by Nov. 23, 1943, the spinal fluid pressure had become normal (120 mm. water). However, on Nov. 27, 1943, he complained of more headache. Spinal fluid pressure was found to be 210 mm. For the first time evidence of right homonymous hemianopsia and astereognosis in the right hand were observed, and the right hemiparesis, which had decreased following the second operation, became more pronounced. Gradually the fungus recurred. Lumbar punctures, performed one to three times a day, revealed pressures of 240 to 280 mm. water with cell counts ranging from 74 to 147. On Nov. 30, 1943, while sitting up smoking, he suddenly lost consciousness, the pupils became dilated and fixed, and stertorous respiration set in. The fungus increased in size rapidly, with much necrotic brain tissue being extruded. In vain the temporal and parietal lobes were tapped with a ventricular needle. No abscess was encountered. Another attempt the following day was successful in reaching a thick-walled abscess cavity in the temporal lobe. However, the patient's course was progressively downward and he died on Dec. 3, 1943. Autopsy revealed a large, well-encapsulated abscess of the left temporal lobe extending into the hippocampal region. No bone fragment was found within the cavity nor in its walls. The metallic foreign body lay one-half inch posterior to the wall of the abscess and was nicely encapsulated.

The mistakes here were incomplete wound débridement initially, and second, failure to employ ventriculography when search for a diagnosed abscess was unsuccessful. If the associated abscess be evacuated relatively early, wound healing and recovery may proceed rapidly, as exemplified in Case 4.

CASE 4.—A 31-year-old infantryman was struck in the left frontal region by a rifle bullet on Oct. 16, 1943. The wound was débrided, the missile removed, and closure effected the following day at a field hospital. A few days later at another institution the wound was observed to have broken down and a fungus was evident. The amount of sulfonamide administered was unknown, and penicillin was not then available. On the patient's arrival



at the Head Center on Oct. 25, 1943, eight days after the initial operation, the wound was found to be draining pus and a tense, shaggy, nonpulsating fungus was present. Neurologic examination revealed mild right hemiparesis and early papilledema. Mental processes were slow, but he was rational, cooperative, and complaining of but slight headache. There was little fever, and the neck was moderately stiff. Roentgenograms revealed several retained bone fragments a short distance beneath the defect in the posterior portion of the left frontal bone.

Under novocain anesthesia the fungus was excised flush with the dura. A mass of necrotic tissue and bone fragments was found beneath, associated with a partially encapsulated abscess. Following evacuation of the latter, and secondary débridement of the wound, the scalp was closed loosely about a drain. Wound cultures revealed aerobic hemolytic *Staphylococcus albus*, and aerobic hemolytic streptococcus. The highest recorded cerebrospinal fluid pressure after operation was 200 mm. of water, with a cell count of 330, of which 40 per cent were polymorphonuclear leucocytes. Convalescence was uneventful and the neurologic recovery apparently complete.

The history of the next patient whose injury was very extensive, illustrates some of the difficulties which may be encountered in the treatment of malignant fungus, where the latter, of itself, is of quite secondary importance. Inadequate débridement, both at the first and at subsequent operations, was apparently responsible for the fatal outcome.

CASE 5.—A soldier was wounded in action in Italy, July 15, 1944, sustaining multiple shell fragment wounds of the left side of the face, left eye, both supraorbital regions, and the right shoulder. There were multiple fractures of both frontal bones, orbital plates, ethmoids and sphenoid, as well as the left temporal and maxillary bones. There was deep injury to both frontal lobes and to the left temporal and parietal lobes. A diffuse shower of coarse and fine bone and metallic foreign bodies extended from the face into the left occipital region. The first operation was performed at an evacuation hospital, where a left frontal craniotomy was done for removal of subdural and extradural clots; in addition, wounds of the face and scalp were débrided and the left eye removed. The large frontal dural opening could not be closed. A gauze pack was placed at the base and brought out through the orbit. The pack was said to have been removed within one week. The scalp incision healed and the patient's general condition improved greatly. However, by July 28 a fungus had filled the defect in the orbital wound through which the pack had been brought out, and a spinal fluid fistula made its appearance there as well.

On arrival at the Neurosurgical Center July 30, 1944, all wounds were healed save the orbit, where the fungus was wet and necrotic. The patient was mentally disturbed and showed many and varied neurologic defects indicative of bilateral cerebral injury, together with signs of impending meningitis. On Aug. 2, 1944, a left temporal craniectomy was performed with removal of subdural and intracortical hematomas, and evacuation of an abscess (nonhemolytic *Staph. albus*). Bone chips and the large foreign body which lay free in a soft, necrotic, pathway leading into the posterior temporoparietal region were removed. This foreign body had been seen to shift position several times in serial films. The poor general condition of the patient prohibited redébridement of the frontal lobe wounds at that time. He improved markedly after this operation, but the fistula about the orbital fungus continued to flow, and because of the danger of meningitis developing he was again operated upon Aug. 8, 1944. On this occasion the fungus and the adjacent necrotic portion of frontal lobe tissue were removed and extensive fascia lata grafts were employed to repair the large dural defects presenting at the opened frontal and ethmoid sinuses. Cultures from the cerebrospinal fluid fistula showed *Bacillus aerogenes* and *Staph. albus*. He did well until Aug. 18, 1944, when his condition became suddenly and temporarily much worse and the scalp flap swelled out under marked tension. The left ventricle was tapped, the fluid cultured, and *Escherichia coli* found. Improvement was again rapid. Sept. 5, 1944, the patient once more suddenly became very ill, and again a ventricular tap yielded a turbid fluid, rich in

cells, with many bacilli and cocci on a stained smear. Sept. 6, 1944, the left temporoparietal lobe was re-explored but no abscess was found. Roentgenograms, meanwhile, had not indicated any shift in any of the remaining foreign bodies. He died on Sept. 9, 1944. Necropsy revealed a mass of seminecrotic tissue between the floor of the left ventricle and the snugly healed dural patch over the orbital roof.

In the light of the next case (Case 6), exploration of the frontal lobe with redébridement should have been done and might well have prevented the patient's death.

That a cerebral fungus associated with a rupture of the ventricle and a wide scalp defect need not invariably be fatal, is illustrated by Case 6.

CASE 6.—A German soldier, aged 19 years, was struck in the left supraorbital region by a .30 caliber bullet on Sept. 20, 1944. The wound was dressed with sulfonamide powder and on the same day he reached one of our evacuation hospitals where the wound was débrided. The large dural defect was repaired with a pericranial graft. The incision, because of loss of tissue, was said to have been closed under great tension. Penicillin was used both locally and intramuscularly (25,000 units injected into the cavity at the close of the operation and 15,000 units injected subsequently each day). Although his general condition improved, a wound infection developed, with colon-smelling pus. Sept. 26, 1944, the wound was opened widely, the exposed portion of the dural graft removed, and pus and necrotic tissue sucked away. A drain was left in the wound. By the following day the temperature had risen to 105° F. and the neck was stiff. Bacteriologic examination revealed "spore-forming anaerobes." Penicillin, 10,000 units, was injected intrathecally each day in addition to that given by routine intramuscular administration. The patient remained comatose until Sept. 29, 1944, at which time the temperature and pulse returned approximately to normal. He began to respond to questions and to take food.

He was then evacuated through two other hospitals, at the latter of which he was seen for the first time by one of us on Oct. 21, 1944. Apparently, he had been holding his own fairly well. Cervical rigidity had disappeared, but pus continued to drain from the wound. Two days previously, cerebrospinal fluid was observed to be issuing from the wound. He then became listless and the temperature rose to 103° F. When seen prior to transfer to the Head Center, the temperature was 104° F., the neck quite stiff, and a large cerebral fungus was present in the left frontal wound, from which there was a copious flow of cerebrospinal fluid. Roentgenographic examination revealed a bone defect 6 cm. in diameter with no retained bone fragments. Cultures from the wound and from the lumbar spinal fluid on at least two occasions disclosed the presence of *Esch. coli*. The cerebrospinal fluid cell count varied from 3,600 to 3,950 cells, with 66 to 72 per cent polymorphonuclear leucocytes.

On Oct. 22, 1944, immediately after admission, a craniotomy was performed under ether anesthesia. After the fungus had been excised, the fistula was seen to extend directly into the anterior horn of the left lateral ventricle. A radical débridement of the left frontal lobe was performed. The frontal sinus was apparently healthy and was not disturbed. The cavity was thoroughly washed with saline solution and 10,000 units of penicillin were instilled. In order to close the huge scalp defect a pedicle flap was brought down from above and the bed of the latter covered by a split-thickness graft placed on the remaining pericranium.

The postoperative course was marked by a temperature rise as high as 102.6° F. the following day, after which it returned to within one degree of normal. From time to time during the next two to three weeks there were episodes of fever and increased fluid under the flap, requiring aspiration. However, the scalp wound healed per primam and the graft took well.

Approximately one month later colon bacillus meningitis recurred. The flap bulged tensely and a re-exploration of the wound was deemed imperative. This was carried out by reopening the lower limb of the old incision. A large smooth-walled cavity was revealed, lined with glistening arachnoidal membrane beneath which numerous silver clips were visible.

No reaction was evident about any of them. The opening into the ventricle was 2 to 3 mm. in diameter; a small mass of seminecrotic tissue containing a few particles of dirt had ruptured through the membrane. This was thoroughly excised back to normal-appearing tissue. The wound was closed as before without drainage. Convalescence from that time on was quite satisfactory, and the patient, when last examined four months after the last operation, was ambulant, without complaints, and with no gross neurologic disturbances.

Cerebral fungi occurred in approximately one-quarter of all deep and superficial infections. The mortality was definitely higher in those deep infections in which fungus developed. They appeared less frequently in those wounds in which the dura had been closed. Hence, dural closure by suture or by living graft is desirable at the time of wound débridement. An additional reason for carrying out this procedure is that the sutured or patched dura may shield the brain effectively from a superficial infection. This has been observed by one of us on at least eight occasions in brain and spinal cord wounds.

#### SUMMARY

1. Thirty-two cases of cerebral fungus which occurred among 426 penetrating skull wounds were studied.

2. These were roughly divisible into two groups: the first, termed "benign," consisted of locally infected herniations associated with superficial wound infections; the second, called "malignant," occurred in conjunction with deeply infected wounds, overlooked hematomas, or pockets of necrotic tissue. In the majority of these the dura had been left unsutured, although in a few it had been forced open by pressure and infection.

3. All save one of the thirteen "benign" fungi were small, grew slowly, and were not associated with progressive neurologic changes. Intracranial pressure was elevated but moderately, if at all. The natural tendency was to heal within a few weeks. Only one, the largest, was excised, and it appeared to have been undergoing fibrosis. Systemic chemotherapy was practiced routinely. There were no deaths in this group.

4. Among the nineteen cases of "malignant" fungus, there were six known deaths and possibly three others subsequent to evacuation. These hernias were large and shaggy with a tendency to bleed. Continued growth of the mass, mounting intracranial pressure, and progression of neurologic changes were characteristic of this group. Treatment entailed evacuation of the abscess or hematoma and/or redébridement of the wound supplemented by systemic sulfonamide and/or penicillin therapy. Excision of the fungus flush with the dura was thus not the essential part of the operation, although it served to lessen pressure in the region of the dural opening<sup>9, 10</sup> and to afford access to the principal source of trouble. In each of the six known fatalities an underlying abscess was overlooked or evacuated too late. With few exceptions these patients can be saved by proper and timely surgical intervention. Systemic chemotherapy with penicillin and/or sulfonamides is apparently of value in preventing meningitis. Should signs of meningeal irritation or invasion appear, penicillin should be employed intrathecally as well, and every effort directed toward elimination of the source of infection. To do less is to court imminent disaster.

5. Case histories exemplifying both successful and unsuccessful treatment are cited, and what are believed to have been the errors committed pointed out.

6. Dural closure, in addition to painstakingly thorough wound débridement at the time of the initial operation, is recommended.

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*The Dr. Walter E. Dandy Birthday Number will be concluded in the June issue of the JOURNAL.*

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## Book Reviews

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**Modern Urology for Nurses.** By S. M. Dwyer, R.N., B.S., and G. W. Fish, M.D. Ed. 2. Cloth. Pp. 287, with 66 engravings. Philadelphia, 1945, Lea & Febiger. \$3.25.

This is a compact volume intended to give the student and graduate nurse the fundamental principles of urologic nursing care. The various problems encountered are well covered and the anatomic, physiologic, and pathologic features of conditions requiring care are discussed so that the nurse should have a comprehensive concept of the underlying disease. Nursing care has then a rational basis and, with understanding, care improves and becomes enthusiastic rather than indifferent.

The chapter on establishment of an urologic section emphasizes the importance of segregation of patients with urologic disorders so that trained staff and special necessary equipment may be available. Throughout the book the necessity of understanding in the treatment of the sensitive, embarrassed patient is stressed and the discussion of the nurses' role in reassurance and teaching of the patient is laudable.

The authors are not dogmatic, but rather give fundamental grounding in urologic nursing care, to be modified by the particular routine of the urologists of any hospital. A description of the necessary staff and required equipment of the Squier Urological Clinic is given in some detail.

The chapter on teaching of urologic nursing seems particularly good. The brief discussions of operative procedures give understanding to the floor nurses and a foundation, to which the urologist should add, to the cystoscopic and surgical nurses.

# SURGERY

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## Dr. Walter E. Dandy Birthday Number

(Concluded)

### PERIPHERAL NERVE INJURIES

#### I. THE RESULTS OF "EARLY" NERVE SUTURE: A PRELIMINARY REPORT

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#### FOREWORD

THE knowledge concerning the biologic and technical factors involved in the repair of peripheral nerve injuries which might have stemmed from the accumulated experience of World War I was almost entirely lost, primarily because no formal follow-up studies of such injuries were initiated. In the interval of peace between that war and World War II little progress was made along these lines because nerve injuries are relatively uncommon in civilian life and even experienced neurosurgeons have difficulty in collecting sufficient clinical material to provide a basis for definitive statements about special techniques.

For these reasons the management of peripheral nerve injuries was little further advanced at the beginning of this war than it was at the end of the last war. Fortunately, however, it was promptly recognized that the opportunities provided in this war would be lost, just as they had been in the last war, if a concerted effort were not made to utilize the mass military neurosurgical experience. The establishment of a Peripheral Nerve Registry for the evaluation of peripheral nerve surgery as it was practiced in Overseas Theaters and in the Zone of the Interior was the outcome of this realization.

The assessment of the end results of this phase of neurosurgery is a long-term endeavor, and sufficient time has not yet elapsed to permit any but preliminary reports. Nonetheless, this first report from the Peripheral Nerve Registry, though it is necessarily inconclusive, makes clear the brilliant results already achieved by the policies laid down for the management of these injuries by the neurosurgical consultants, whose policies were, in turn, the result of the policies of specialization of personnel and concentration of specialized material under which the surgical consultants division of the Surgeon General's Office has operated since its inception. This preliminary report also makes clear the

valuable contributions which will continue to flow from these studies, the lessons of which are readily applicable to civilian neurosurgery.

Without the cooperation of the neurosurgeons in the Theaters of Operations and the Zone of the Interior the Peripheral Nerve Registry could not have succeeded. Approximately 5,000 peripheral nerve sutures have now been recorded, and a steadily increasing number of assessments is being received in the Surgeon General's Office. The contemplated transfer of the Registry to the Veterans' Administration and the further study of nerve regeneration under its auspices should permit conclusive results concerning this phase of neurosurgery during the coming years.

FRED W. RANKIN

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**I**F THE great mass of war casualties suffering from peripheral nerve injuries could have been transported and distributed rapidly to the general hospitals designated as neurosurgical centers in the Zone of the Interior (the continental United States), there would have been no indication for an integrated attack overseas upon this special problem. Since many casualties could not be transported for various reasons, both physical and tactical, it was necessary to develop in overseas installations a program of treatment designed to promote for each individual patient a maximal chance for rehabilitation. "Early" nerve suture as practiced in the neurosurgical centers of the United Kingdom was, therefore, in large part a phase of military neurosurgery. It will be apparent, however, that the experience gained in its use is readily applicable to nerve suture performed in a more desirable environment.

By successive directives and technical reports<sup>1-5, 13</sup> the care of a peripheral nerve injury sustained in combat was divided into two distinct phases. The first included the preservation of the extremity as a whole and the prevention of infection, which was achieved by débridement and by delayed wound closure. Whenever possible, at either the first or the second of these procedures, divided peripheral nerve tissue was coapted by a radiopaque suture and was protected from the pressure of dressings by contiguous muscle or fascial tissue. At such operations the extensive mobilization and transplantation dissections which are essential in restoring nerve defects were regarded as contraindicated by the probability of subsequent infection. If nerve suture is attempted under these circumstances, recourse must be made to joint posturing which is often unphysiologic in extent, and the thin, friable epineurium characteristic of a freshly divided nerve and the necessary postoperative stretch upon the site of suture are further technical factors prejudicial to successful axonal regeneration.

The second phase of the care of a peripheral nerve injury sustained in combat has to do with reconstructive surgery, including definitive suture, physiotherapy, and the observation of regeneration. As the time period from the injury lengthens, however, progressive deterioration occurs in the distal nerve segment, characterized by epineural, perineural, interfascicular, and endoneural fibrosis, by nerve bundle atrophy, and by an irregular tubule atrophy leading

rapidly to complete obliteration of the tubule cross-section area.<sup>7</sup> When to these changes are added muscle atrophy, nerve ending degeneration, and peri-articular fibrosis, the barrier to nerve regeneration after a three-month period becomes increasingly formidable. Early nerve suture, as practiced by overseas military neurosurgeons, was designed to take advantage of the favorable time period commensurate with optimum nerve regeneration, that is, not earlier than three weeks and not later than three months after nerve injury.

Early nerve suture is influenced under military conditions by many circumstances other than the obvious ones of a complicated injury and the pressure of bed evacuation. At least three other factors had to be taken into consideration, namely, properly trained personnel, their technical dexterity, and the varying immediate response of a peripheral nerve to an inflicting force.

The present communication is concerned entirely with an effort to establish or disprove the value of early nerve suture as a military neurosurgical procedure, keeping in mind the major influence of time after injury and the subsidiary factors already noted. Successive reports will be concerned with such other data as ballistic studies, the bone, vessel, and soft tissue complications of peripheral nerve injuries, regeneration in special nerves, and the duration of hospitalization for nerve injuries.

#### THE PERIPHERAL NERVE REGISTRY

In an endeavor to evaluate the influence of standardized procedures and newly developed technical advances upon the end results of peripheral nerve repair, a Peripheral Nerve Registry was established by the Surgeon General Nov. 22, 1944.<sup>6</sup> At first the Registry was maintained only in the nineteen general hospitals in the Zone of the Interior designated for the care of neurosurgical casualties, all of which were headed by diplomates of the American Board of Neurological Surgery. Later the initiating forms were extended to overseas installations. The maintenance of the Registry and the compilation of reports, which are submitted every three months, was made the responsibility of the neurosurgical staffs of the various centers, and the present report is the result of the efforts of eighty-five reporting surgeons.

Certain facts concerning the Registry should be emphasized. In the first place, it was designed for specialized studies which can be carried out only by medical personnel trained in neurosurgery and which extend far beyond the confines of purely statistical data. Statistical studies as such are the function of the Surgeon General's Office.

In the second place, as will be observed from Tables I to XII, few of the clinical categories are complete on all forms received. In part the omissions are due, as is true of all similar studies, to careless recording. There are, however, more pardonable reasons. One is that in combat areas careful initial observations were frequently not possible, for obvious reasons. Another is that even on higher levels a large amount of paper work is required in all hospital installations and there is a limit to the capacities of an observer, no matter how great his enthusiasm. While it would have been desirable in many instances



TABLE I. NERVE INVOLVEMENT AND TYPE OF END-TO-END ANASTOMOSIS (ORIGINAL DEFINITIVE PROCEDURE) IN 669 NERVE INJURIES SUSTAINED BY 563 CASUALTIES\*

NERVE INVOLVED	PREVIOUS BULB SUTURE		TYPE NOT STATED	TOTAL	PROPORTIONATE DISTRIBUTION
	WITH	WITHOUT			
Ulnar	5	181	29	215	32.3
Sciatic		105	24	129	19.3
Median		98	16	114	17.0
Radial	2	83	11	96	14.4
Peroneal		55	13	68	10.1
Tibial		18	1	19	2.8
Musculocutaneous		8	1	9	1.3
Brachial plexus		6	2	8	1.2
Facial		1		1	0.1
All others		8	2	10	1.5
Total injuries	7	563	99	669	100.0

\*Three instances in which nerve grafting was the original definitive procedure (ulnar, radial, sciatic) are not included in this table.

to have more complete data, those supplied were, on the whole, ample for the purposes of this study.

In the third place, the Registry forms, although necessarily detailed, were deliberately kept as simple as possible. This is particularly true of the assessment of degrees of recovery, in which the categories were adopted, with only minor changes, from those which the British, with a much longer experience, had found to be practical. A Registry designed for the recording of a potential reservoir of many thousands of cases obviously cannot be devoted to minutiae, however attractive such an analysis might be. That task must be reserved for single observers studying personal series of cases.

Finally, of the many difficulties inherent in the appraisal of neural regeneration after suture, not the least is the prolonged time interval required for successful neural regeneration to be finally assessed. This difficulty has been met in part by requiring that assessments of all cases in the Registry be submitted at successive three-month intervals. On the other hand, the recognition of frank failures or of variations from the usual tranquil course of axonal regeneration demands only the presence of trained observers and a central means for assembling pertinent data.

The Peripheral Nerve Registry Report S. G. Form 941 provides for the reporting of the following data:

A. Identification and administration, including the name of the general hospital; the hospital and the Peripheral Nerve Registry serial numbers; the patient's name, Army Serial Number, organization, and arm or service; the dates of his admission, operation, and discharge and the date of the report; the name of the operating surgeon; the type of admission (original or readmission); the date of the patient's disposition to full or restricted duty, or of the certificate of disability for discharge or retirement, or of transfer to another type of hospital installation; the total time lost from duty and the lapse of time before operation and disposition.

TABLE II. INCIDENCE OF SINGLE AND MULTIPLE NERVE INJURIES

INJURIES	CASES	PROPORTION
Single	659	91.9
Multiple	50	8.1
Total	619	100.0

TABLE III. CAUSATIVE AGENT IN 595 BATTLE AND 25 ACCIDENTAL PERIPHERAL NERVE INJURIES

AGENT	CASES	PERCENTAGE
Shell or bomb fragment, shrapnel	385	62
Gunshot wound or bullet	160	26
Accidental	25	4
Land mine, booby trap, grenade	17	3
Unspecified	33	5

B. The date, cause, and location of the injury, and the nerve or nerves involved.

C. The operative findings. Since the Registry was set up for a study of nerve suture and nerve grafting, operative findings are limited to the measurement in centimeters of the nerve defect or gap before surgery, that is, before surgical dissection, and after surgery, that is, after pathologic tissue has been resected and the extent of the defect or gap is evident.

D. Pathologic findings, stated in such established terms as proximal or lateral neuroma, distal glioma, anastomosis line, neuroma in continuity, and graft.

E. Operative details including, according to whether nerve suture or nerve graft was done, the type of dissection (mobilization, transplantation, bone resection, etc.); the type of suture (primary, bulb, secondary, tertiary, etc., and complete or partial); the suture material; the use of stay sutures; the use and method of application of nerve sheaths or cuffs; the type of graft (full thickness, cable); the derivation of the graft (autogenous, homogenous, heterogenous); the character of the graft (fresh, predegenerated, fixed, dehydrated); the technique of insertion; and other pertinent details in the particular case.

F. Assessment of motor recovery in the following terms:

0. No contraction.

1. Perceptible contraction in proximal muscles.

2. Same as No. 1 plus return of perceptible contraction in distal muscles to such a degree that sufficient power is present to act against resistance.

3. Same as No. 1 and No. 2 plus return of synergic and isolated movements.

4. Complete recovery.

G. Assessment of sensory recovery in the autonomous zone in the following terms:

0. Absence of sensibility.

1. Recovery of deep cutaneous pain.

2. Recovery of some degree of superficial pain and touch.

3. Recovery of pain and touch without overresponse.

4. Same as No. 3 plus recovery of 2-point discrimination.

H. The progressive descent of Tinel's sign recorded in centimeters.

I. Data as to the influence of bone, blood vessel, and extensive soft tissue (plastic) injury, intraneural pathologic changes, overseas procedures, and other factors which might influence the course of neural regeneration.

TABLE IV. ASSOCIATED LOCAL DAMAGE IN 621 PERIPHERAL NERVE INJURIES

TYPE OF DAMAGE	NUMBER OF CASES	PROPORTION OF REPORTED CASES
Bone	80	21.7
Vascular	47	12.7
Soft tissue*	4	1.1
Bone and Vascular	5	1.3
Bone and soft tissue	4	1.1
None	229	62.3
Unknown or unreported	252	

\*Counted as such only in instances of marked loss of substance or severe infection requiring plastic procedures.

The original assessment of recovery as defined by electrical percutaneous studies was based upon the simplified classification devised by de Jong.<sup>9, 10</sup> The studies usually conducted in Army installations, aside from certain other disadvantages, are complicated for purposes of record. They were also designed

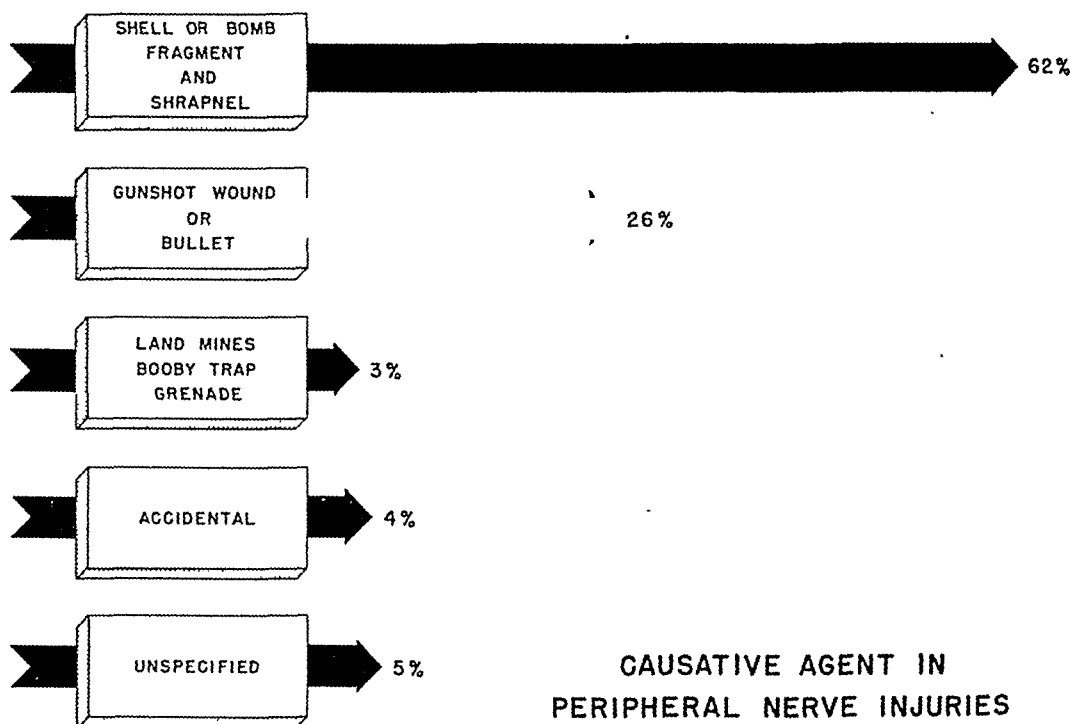


Chart A.

to be transposed at some future date in terms of the promising galvanic-tetanus ratio studies conducted by Pollock and his associates<sup>11</sup> among Army casualties. This method, and the equally provocative skin resistance studies of Whelan and Richter<sup>15</sup> and of Jasper and Robb<sup>8</sup> have therefore been placed in the Registry but to date have not been made mandatory.

#### MATERIALS AND METHODS

During the interval between D-Day, June 6, 1944, and V-E Day, May 8, 1945, 6,245 casualties with peripheral nerve injuries were admitted to the twelve neurosurgical centers established in the United Kingdom and operated under the over-all direction of Colonel R. Glen Spurling, Senior Consultant in Neurosurgery, European Theater of Operations. Operation was performed in 2,873 of these cases.<sup>14</sup> In 1,319 cases, procedures described as external or internal neurolyses were carried out. In the remaining 1,554 cases (54.1 per cent) peripheral nerve division was encountered and end-to-end suture was accomplished.\* These operations were performed on an average of thirty-nine days

\*This analysis also includes a small number of cases handled in other theaters of operations.

TABLE V. PROPORTIONATE DISTRIBUTION IN RESPECT TO TIME INTERVAL BETWEEN WOUNDING AND DEFINITIVE NEUROSURGERY IN 661 CASES

TIME INTERVAL (DAYS)	ACTUAL CASES	PERCENTAGE	CUMULATIVE CASES	PERCENTAGE
Wounding	63	9.5	63	9.5
6	22	3.3	85	12.8
12	13	2.0	98	14.8
18	16	2.4	114	17.2
24	31	4.7	145	21.9
30	37	5.6	182	27.5
36	66	10.0	248	37.5
42	74	11.2	322	48.7
48	68	10.3	390	59.0
54	50	7.6	440	66.6
60	48	7.3	488	73.9
66	26	3.9	514	77.8
72	21	3.2	535	81.0
78	34	5.1	569	86.1
84	26	3.9	595	90.0
90	12	1.8	607	91.8
120	33	5.0	640	96.8
150	10	1.5	650	98.3
180	1	0.2	651	98.5
Over 180	6	0.9	657	99.4
Unknown	4	0.6	661	100.0

TIME INTERVAL BETWEEN WOUNDING AND NERVE SUTURE

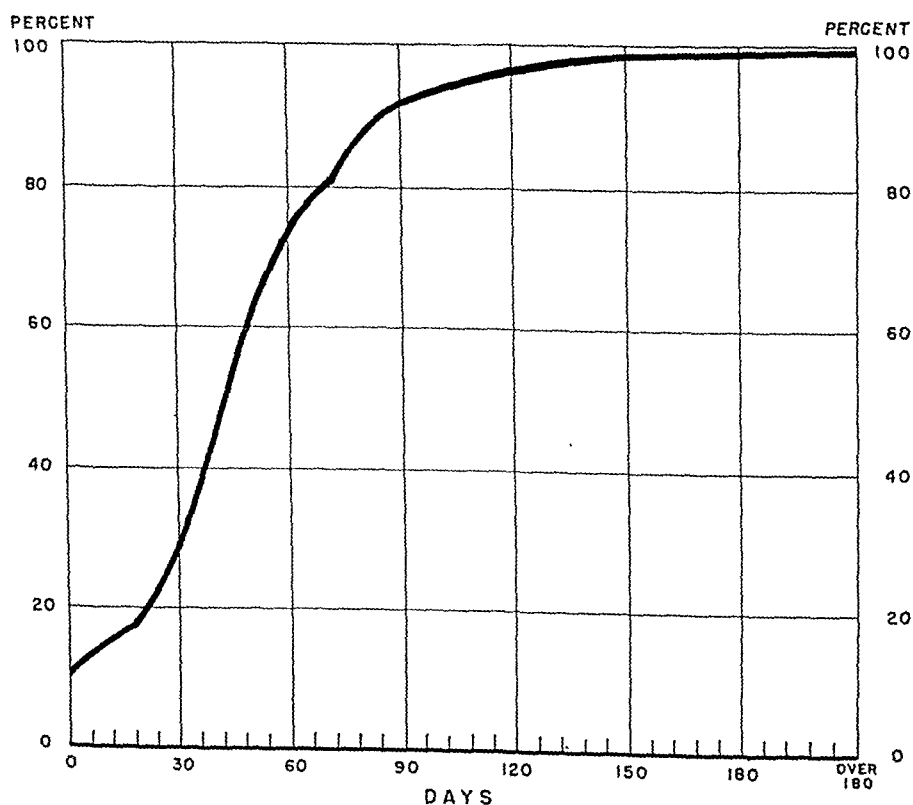


Chart B.

TABLE VI. TECHNIQUE OF END-TO-END ANASTOMOSIS IN 648 OPERATIONS FOR PERIPHERAL NERVE INJURIES\*

TECHNIQUE	NUMBER OF CASES	PROPORTION OF REPORTED CASES
Complete	585	90.3
Partial	63	9.7
With tantalum wire	448	75.1
Other suture material	141	23.6
Both	8	1.3
With stay suture	191	42.5
Without stay suture	258	57.5
Wrapped in tantalum foil	374	97.9
In other material	8	2.1
With mobilization	263	72.6
Transplantation	47	13.0
Both	52	14.4
With bone resection	4	

\*Only positive (stated) data are included under each heading.

after the injury. While the total number of peripheral nerve operations carried out at the time of injury or shortly afterward in evacuation hospitals or other facilities of this type is not known, eighty-nine have been recorded, which is a sufficient number to make possible a comparison of results between this practice and the practice just described as early nerve suture.

The following methods of analysis were employed:

1. Significant samples of cases of early nerve suture, ranging from 450 to 649, were chosen for study as the records appeared successively in the Registry. The period of observation after operation in these groups ranged from three to twelve months and the instances of early if incomplete regeneration included in the analysis represent instances of incomplete nerve division. The initiating forms and assessments were coded and from these cards the statistical studies reported in Tables I to XI were derived. Since each study was of a specialized character, the total number of cases varies to some degree in each individual compilation.

2. In order to compare the validity of results obtained in neural regeneration as demonstrated by the coding and statistical analysis of a large group of cases within the specifications of the Registry and of a smaller group analyzed

TABLE VII. RATE OF MOTOR RECOVERY BASED ON MONTHLY POSTOPERATIVE ASSESSMENTS IN 649 STATED CASES OF PERIPHERAL NERVE INJURY

POSTOPERATIVE TIME INTERVAL (MONTHS)	RECOVERY CODE				
	0	1	2	3	4
1.9	54	5	2		
2.9	67	6	3		
3.9	133	21	7	3	1
4.9	71	11	6	3	
5.9	32	13	6	5	
6.9	32	25	14	8	1
7.9	14	9	5	4	
8.9	10	9	4	4	
9.9	9	16	8	3	
10.9		3	1	2	
11.9		1	2	2	
12 and over	5	4	1	3	1
Total number assessments	427	123	59	37	3

TABLE VIII. RATE OF SENSORY BASED ON MONTHLY POSTOPERATIVE ASSESSMENTS IN 649 STATED CASES OF PERIPHERAL NERVE INJURY

POSTOPERATIVE TIME INTERVAL (MONTHS)	RECOVERY CODE				
	0	1	2	3	4
1.9	55	5	3		
2.9	64	8	1	1	
3.9	133	22	8	3	
4.9	70	11	6	3	
5.9	39	10	4	2	
6.9	33	22	20	6	
7.9	18	5	6	2	1
8.9	13	9	6		
9.9	18	13	5	1	
10.9	1	1	3	1	
11.9		1	3	1	
12 and over	3	2	3	4	
Total number assess- ments	447	109	68	24	1

by a single individual ("hand" analysis), 450 cases of nerve repair were selected for this purpose, distributed evenly among a group ranging, as to the time lapse, from those reported shortly after the Registry was implemented to those reported less than three months prior to this study. If hand analysis has any advantage over other methods it lies in the personal experience of the analyst and the uniformity of the personal equation.

3. The hand analysis was then extended to 602 cases, including the 450 originally studied by this method. Each instance of failure in this larger group was studied in detail and so far as possible material was secured in each case for pathologic study. The results of this inquiry are reported in Table XII and illustrative case reports are appended.

Assessment of the first group of cases (450) studied by hand analysis produced the following results:

*345 patients showed evidence of nerve regeneration, divided as follows:*

110 patients showed progressive descent of Tinel's sign, with evidence of motor regeneration ( $M_1$  or higher) and of sensory regeneration ( $S_1$  or higher).

TABLE IX. INTERVAL BY MONTHLY ASSESSMENTS BETWEEN OPERATION AND FIRST APPEARANCE OF TINEL'S SIGN IN 571 STATED CASES

POSTOPERATIVE TIME INTERVAL (MONTHS)	PRESENT			NEVER PRESENT	TOTAL ASSESSMENTS
	EARLIER ASSESSMENT	LATEST ASSESSMENT	TOTAL		
1.9		38	38	19	57
2.9		53	53	20	73
3.9	4	129	133	24	157
4.9		61	61	22	83
5.9		39	39	8	47
6.9	9	50	59	9	68
7.9	1	20	21	4	25
8.9	1	18	19	3	22
9.9	1	19	20	1	21
10.9		3	3		3
11.9		2	3		3
12 and over	1	6	7	5	12
Total	18	438	456	115	571

33 patients showed progressive descent of Tinel's sign, with evidence of motor regeneration ( $M_1$  or higher).

28 patients showed progressive descent of Tinel's sign, with evidence of sensory regeneration ( $S_1$  or higher).

163 patients showed progressive descent of Tinel's sign.

3 patients showed motor regeneration ( $M_1$  or higher).

2 patients showed sensory regeneration ( $S_1$  or higher).

6 patients, although they presented none of these signs, showed gross evidence of nerve regeneration when surgical exploration was carried out.

### RATE OF NERVE REGENERATION

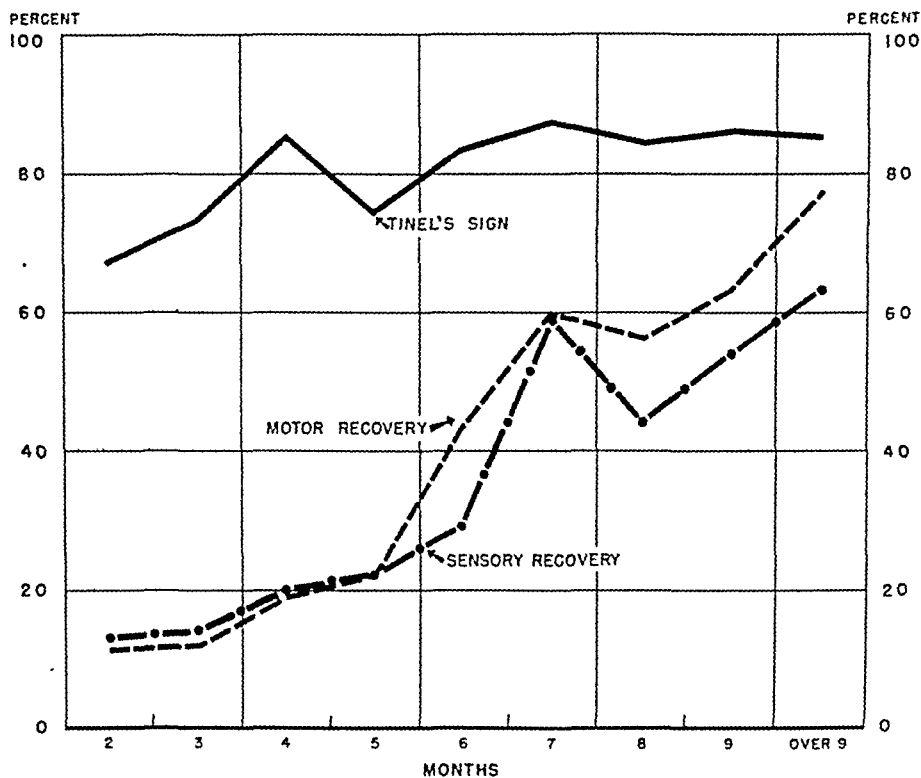


Chart C.

53 patients presented no evidence of nerve regeneration, divided as follows:

17 patients showed evidence of suture failure.

2 patients showed evidence of graft failure.

34 patients showed no evidence of regeneration in periods ranging from three months in 26 cases to nine months in 2 cases.

In the remaining 52 cases, the time interval after suture was less than three months in 19 cases, while in 33 others no report after operation was available.

The analysis of the 398 cases in which the appropriate data were available showed some degree of regeneration evident after three months in 86.7 per cent

TABLE X. INTERVAL BETWEEN OPERATION AND FIRST EVIDENCE OF MOTOR AND SENSORY RECOVERY IN 571 STATED CASES

INTERVAL IN MONTHS	EVIDENCE OF RECOVERY				NO EVIDENCE OF RECOVERY		TOTAL RECOVERIES		TOTAL ASSESSMENTS	
	PREVIOUS ASSESSMENTS		LAST ASSESSMENTS		MOTOR	SENSORY	MOTOR	SENSORY	MOTOR	SENSORY
	MOTOR	SENSORY	MOTOR	SENSORY						
1.9			6	8	48	48	6	8	54	56
2.9			9	10	62	60	9	10	71	70
3.9	3	2	29	31	110	109	32	33	142	142
4.9		1	18	18	60	59	18	19	78	78
5.9	3		20	16	29	34	22	16	51	50
6.9	9		39	38	29	24	48	47	77	71
7.9	2	2	13	11	13	19	15	13	28	32
8.9	1	3	12	11	10	12	13	14	23	26
9.9	4	4	14	8	9	16	18	12	27	28
10.9	2	2	4	4			6	6	6	6
11.9	1	1	2				3	1	3	1
12 and over	1	2	5	5	5	4	6	7	11	11
Total assess- ments	25	26	171	160	375	385	196	186	571	571

of all cases (345) and potentially unfavorable results in 13.3 per cent (53). The proved failures in 417 follow-up cases (including the 19 cases in which the time lapse after suture was less than three months) numbered 19, or 4.5 per cent. The results in the 450 cases analyzed by the hand method show a remarkably close correlation with the 649 cases analyzed by the statistical methods employed in the evaluation of the Registry cases (Table VII).

The hand analysis carried out on the larger number of cases (602) needs no special comment except that the 5.0 per cent of failures (21 of 419 cases) which occurred in general hospitals is worth emphasizing, in view of the principles laid down for nerve suture, in contrast to the 22.4 per cent of failures (20 of 89 cases) which occurred in advanced units (Table XII).

It is realized that the maximal period of observation in these cases, twelve months, is short for the assessment of full nerve regeneration, but it is sufficient to show the trend of normal nerve growth. Frank failures, on the other hand, are clearly manifest during a period of observation of this length. The 44 failures which occurred in 602 instances of early nerve suture reported in the

TABLE XI. INTERVAL BETWEEN OPERATION AND FIRST APPEARANCE OF TINEL'S SIGN IN 571 OPERATIONS FOR PERIPHERAL NERVE INJURY\*

INTERVAL IN MONTHS	SIGN PRESENT		SIGN NOT PRESENT		TOTAL ASSESSMENTS
	CASES	PROPORTION	CASES	PROPORTION	
1.9	38	60.3	25	39.7	63
2.9	91	66.4	46	33.6	137
3.9	234	75.4	73	24.6	297
4.9	285	74.6	97	25.4	382
5.9	324	75.3	106	24.7	430
6.9	383	78.2	107	21.8	490
7.9	404	78.6	110	21.4	514
8.9	423	79.2	111	20.8	534
9.9	443	79.8	112	20.2	555
10.9	446	79.8	113	20.2	559
11.9	449	80.0	112	20.0	561
12 and over	456	79.9	115	20.1	571

\*The figures and proportions are cumulative and represent the total and proportionate number of cases assessed up to the stated interval.



TABLE XII. DISTRIBUTION OF FAILURES IN RELATION TO HOSPITAL INSTALLATIONS IN EARLY NERVE SUTURE

INSTALLATION	CASES	FAILURES	PROPORTION
General hospital	419	21	5.0
Forward installations	89*	20	22.4
Installation unknown	94	3	
Total	602	44	7.3

\*Evacuation hospitals 53, other advanced units 36.

Registry were therefore studied in detail, as already mentioned, in an endeavor to determine the cause of the unsuccessful results. Whenever possible, material was secured for pathologic study.

From the standpoint of the time at which repair was done these cases fall into three groups:

- (1) 16 cases in which repair was done at the time of wound débridement.
- (2) 3 cases in which repair was done at the time of delayed wound closure.
- (3) 16 cases in which repair was done shortly after delayed wound closure.

In the remaining nine cases the failures can be ascribed to various causes which bear no relationship to the time at which repair was done.

Case reports representative of each of these groups of failures are appended and are preceded by reports of cases in which regeneration preceded normally.

#### CASE REPORTS\*

##### *Successful Nerve Suture Eighteen Days After Injury*

CASE 1 (B. G. H.).—A soldier received a mortar shell fragment wound of the right upper arm, with division of the median and ulnar nerves, May 23, 1944. After delayed wound closure both nerves were sutured June 10, 1944. No details concerning the operation were contained in the overseas clinical records. At the first Registry report Feb. 5, 1945, a progressive descent of Tinel's sign was recorded. At the second report June 12, 1945, the descent amounted to 57.5 cm., an average rate of 1.7 mm. per day, which corresponds rather closely with figures derived from more exactly conducted clinical studies.<sup>12</sup> At this time some degree of functional restoration was also evident.

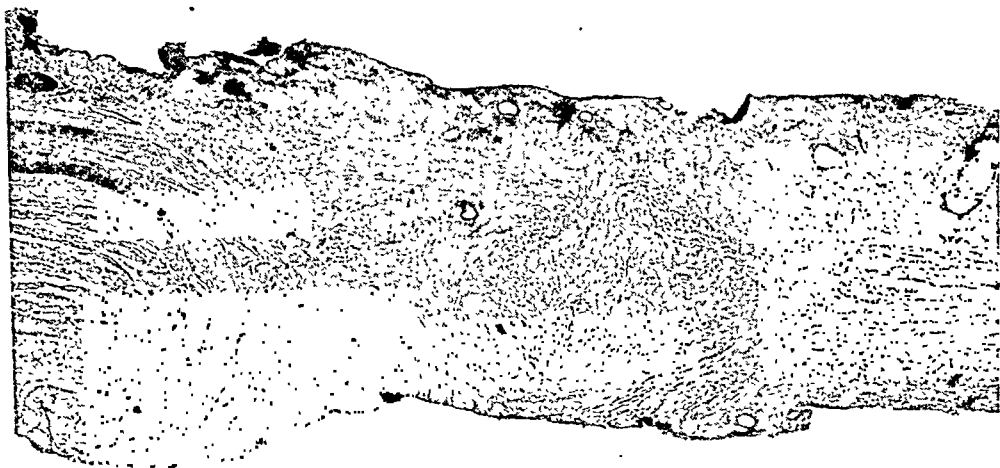
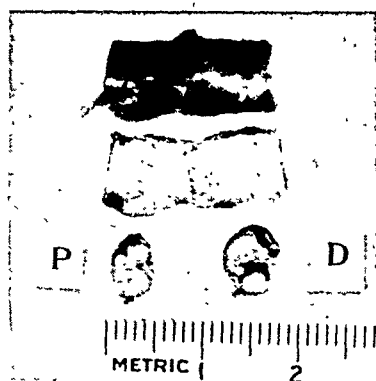
##### *Successful Nerve Suture in Combined Bone-Peripheral Nerve Injury Forty-One Days After Injury*

CASE 2 (PNR 138, L. G. H.).—A soldier received a shell fragment wound of the right thigh Feb. 20, 1944, with a compound fracture of the femur and a division of the sciatic nerve. Débridement was performed and a hip spica applied February 21. Five days later the cast was removed, delayed wound closure was done, and balanced traction was instituted. Four Steinmann pins were inserted and a Roger Anderson external splint was applied April 7. The following day the defect in the sciatic nerve was sutured with black silk and a full leg cast was applied, in which the Steinmann pins were incorporated. The splint and pins were removed May 8 and a new cast was applied. Function in the gastrocnemius and soleus muscles was first noted Nov. 23, 1944, and by Jan. 5, 1945, was 25 per cent of normal. By May 21, 1945, plantar ankle flexion was estimated at 75 per cent, although there was still no evidence of function in the flexor digitorum longus or flexor hallucis longus. The peroneal musculature was also still paralyzed, but the sensory zone of the common peroneal nerve showed an S<sub>1</sub> response and there has been a progressive descent of Tinel's sign to the level of the tibial condyles over the course of both sciatic components.

\*Each patient is identified by the Peripheral Nerve Registry number and initials of the particular hospital in the Zone of the Interior in which treatment was carried out.

*Comment.*—These two cases have been selected for presentation for two reasons: (1) Both suggest the progressive, uneventful course of nerve regeneration exhibited in the majority of cases of early suture reported in the Registry. (2) Both indicate, even in the abbreviated form in which they are presented, the many-sided responsibility of the overseas military neurosurgeon who performs early nerve suture and then transfers his patient to the Zone of the Interior for rehabilitation. In Case 2 minute details of treatment are available, and an intelligent assessment of therapy and of therapeutic results is possible. In Case 1 the record is lacking in all details, including any definition of the term "suture." These errors of omission occurred in many of the cases studied and added greatly to the difficulties of assessment and analysis.

A.



B.

Fig. 1 (Case 3).—A, Gross specimen showing site of initial coaptation and nerve ends obtained at secondary neurorrhaphy. B, Median longitudinal section showing dense scar tissue, neuroma filling in old breach, fascicles forming lateral neuroma, and remnants of coapting suture.

*Coaptation Nerve Suture One Day After Injury, Definitive Suture Fifty-Nine Days Later*

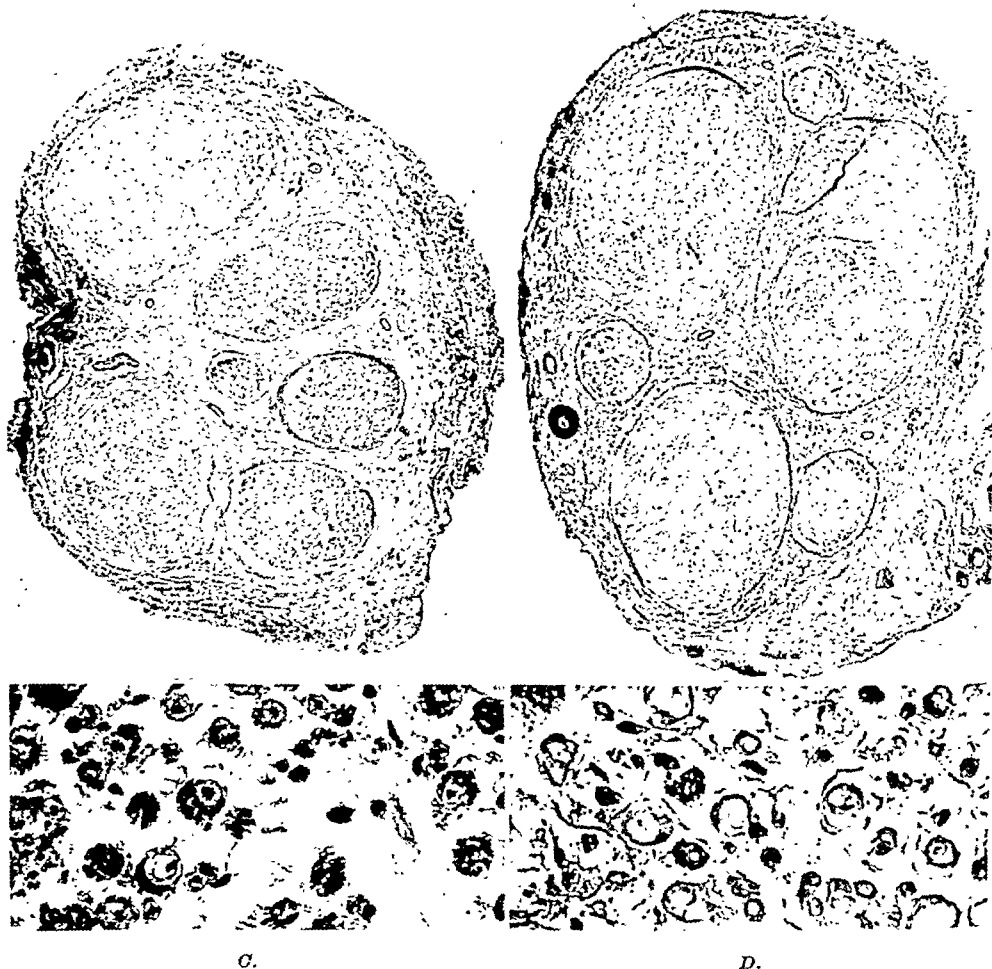
CASE 3 (PNR 140, H. G. H.).—A soldier received a machine gun bullet wound of the left arm March 2, 1945. Débridement was done the following day. The radial nerve, accord-

ing to the record, was "incompletely lacerated," but no mention was made of any type of nerve suture. Because of the lack of a definite record of treatment, re-exploration was carried out May 1, 1945.

The radial nerve was first recovered distally between the brachialis and brachioradialis muscles. Stimulation at this time produced no motor response distal to the lesion, although a locally painful sensation radiated down the arm. The nerve was then followed upward until the point of scarring was encountered. The lateral head of the triceps was partially taken down at its origin, thus exposing the nerve as it emerged from the humeral groove. Stimulation of the isolated nerve produced the anticipated pain response but failed to produce any motor response. The area of scarring, which was rather narrow, was freed from the adjacent tissues by sharp dissection, and the nerve was found to be quite firm in this region. Because of the absence of motor response it was concluded that the few nerve

A.

B.



C.

D.

Fig. 2 (Case 3).—A, Cross section of proximal nerve segment showing slight epineurial and perineurial thickening and intrafascicular fibrosis and edema ( $\times 22.5$ ). B, Cross section of distal nerve segment showing slight epineurial and perineurial fibrosis, and heavy silk suture in epineurial tissue ( $\times 22.5$ ). C, Higher magnification showing edema and light mucoid fibrous process separating nerve fibers. Some fibers appear normal and myelinated and others degenerated and vacuolated. Small regenerating, amyelinated neuraxes are seen in clusters in tubular walls and intertubular areas ( $\times 600$ ). D, Higher magnification showing unshrunk tubules still containing unresorbed detritus. Some of the fine black dots in the tubular walls and intertubular regions are cross sections of a few of the axones which penetrated the zone of scar tissue ( $\times 600$ ).

fibers present represented a downgrowth rather than a sparing, and that they should be sacrificed. The nerve was, therefore, divided by serial section proximally and distally until healthy fascicles were encountered; the defect then measured 2.5 cm. With flexion of the elbow end to end suture could be performed without undue tension.

The specimen (Figs. 1 and 2) was reported as a neuroma in continuity. Histologic examination revealed dense fibrosis at the zone of suture; neuroma formation; slight regeneration of nerve fibers across the junction into distal tubules still in a degenerative resorptive phase; edema; and slight endoneurial fibrosis in the most distal section.

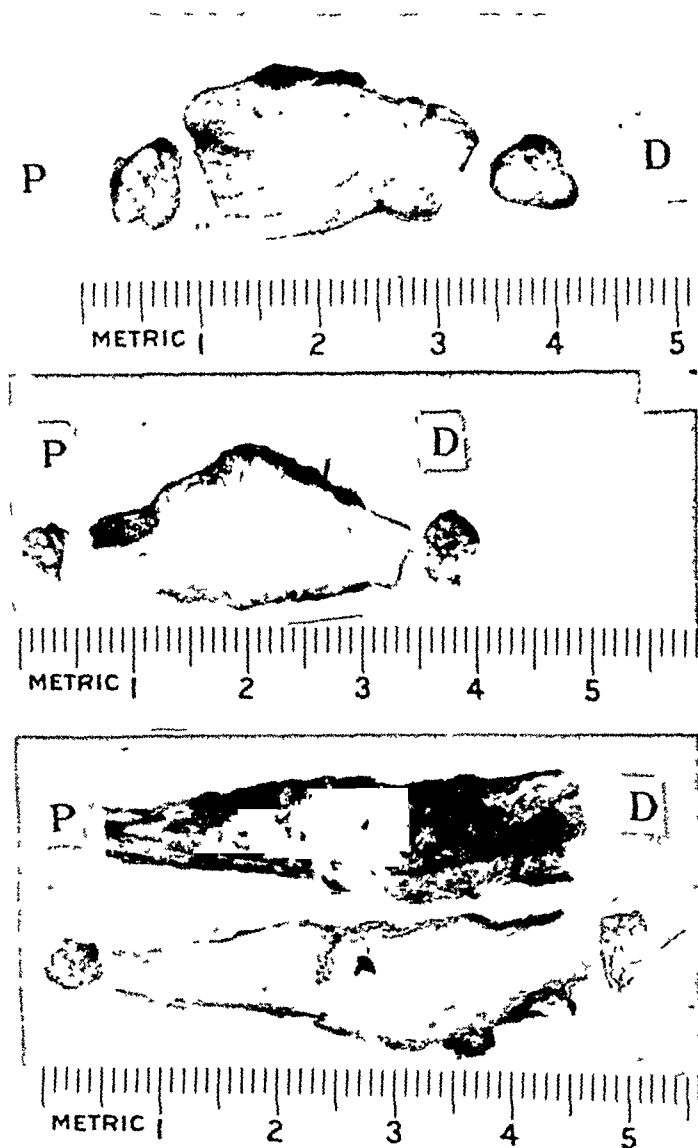


FIG 3—Gross specimens showing coaptation sutures removed at definitive neurorrhaphy in various cases, note the relatively normal appearance of the proximal and distal nerve segments.

*Comment.*—Except for the failure to mention in the overseas (field) medical record that a coapting suture had been placed in the epineurium of the almost completely severed nerve when débridement was done the day after injury, the

handling of this case appears to have been excellent. The badly injured nerve was approximated with a temporary suture so placed as to cause no additional damage to any of the nerve fascicles later to be approximated at definitive surgery. Two months were permitted to elapse before secondary nerve suture was done, a period of time which was not excessive judging by the nerve ends attained after resection of the lateral neuroma and of a 2.5 cm. length of the suture line. The fascicles at both ends were large and edematous, but only a minimum of epineural and intraneural scarring had occurred. Retrograde degeneration had occurred in some fibers for a distance of at least 1 cm. from the point of severance, and many clusters of regenerating neuraxes had already formed. The distal tubules were still widely patent, and the endoneural collagenizing process which had begun was slight. The relatively few and sparsely distributed amyelinated neuraxes which had grown into the distal nerve segment were ample to transmit the electrical impulse applied at surgery, but this finding was properly interpreted and disregarded by the surgeon, whose decision to perform total resection was based upon the appearance and consistency of the lesion and the obscurity of the overseas record in respect to whether or not true suture had been performed. The motor deficiency played less part in the decision because the time lapse was only two months.

The eventual favorable course of events in this case indicates to some extent the method of treatment to be applied when peripheral nerve division is visualized at the time of wound débridement. This point will be emphasized later by reference to the high percentage of failures which follow more ambitious procedures at this time. A coaptation suture, if it is feasible, retains the peripheral nerve structures in recognized tissue planes, and well documented pathologic studies suggest that it delimits the extent of secondary resection of pathologic tissue necessary to achieve a satisfactory definitive suture. The histologic status of the distal segment in this case should be compared with the advanced deterioration present in Case 11 (Figs. 9 and 10), which must be considered a barrier to full regeneration.

#### *Nerve Suture With Débridement; Error in Tissue Identification*

CASE 4 (PNR 16, W. R. G. H.).—A soldier sustained a shell fragment wound of the posterior aspect of the right thigh, with injury to the sciatic nerve, July 13, 1944. When débridement was done an unspecified "suture" of the exposed sciatic nerve was also done; this may have been a coaptation suture. The dubious clinical history and the lack of any descent of Tinel's sign were regarded as sufficient indications for re-exploration, which was done Oct. 3, 1944. The distal segment of the sciatic nerve was found to have been sutured to the tendon of the semitendinosus muscle. End-to-end anastomosis was carried out, and assessment June 21, 1945, suggested beginning regeneration.

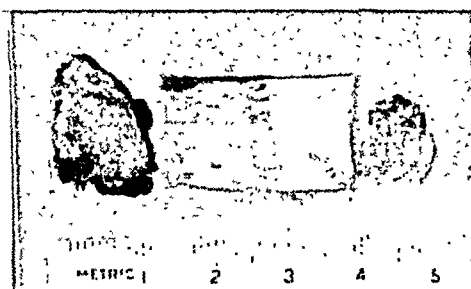
#### *Exploration of Lesion in Continuity at Delayed Wound Closure; Assumption of Spontaneous Regeneration; Failure of Regeneration Thirteen Months After Injury*

CASE 5 (PNR 262, B. G. H.).—A soldier received a bomb fragment injury of the middle third of the left forearm May 8, 1944, with injury to the median nerve. At delayed wound closure exploration of the median nerve injury suggested, on the basis of gross examination, that spontaneous regeneration was possible, and no operative procedure was carried out. Observation over a period of thirteen months showed no evidence of neural growth through the point of injury. Exploration was therefore carried out June 27, 1945. Stimulation of

the distal segment elicited a minor sensory response but no evidence of motor function, and resection of 10 cm. of neural tissue was necessary before normal-appearing nerve tubules could be secured for definitive suture.

*Comment.*—Failure to recognize pathologic changes in a freshly injured nerve, even though such changes may progress to extensive neuroma formation, is not a measure of a neurosurgeon's ability. In 45.9 per cent of the clinically complete nerve lesions which were explored in the neurosurgical centers of the United Kingdom the nerve appeared in continuity. The import of the failures, however, which numbered only two in this particular series of forty-four failures, is the need for a clear operative note and the necessity of following with scrupulous care the clinical course of all nerve sutures performed overseas.

A.



B.

FIG. 1 (Cont'd). A, Median horizontal section of anastomotic site of neurorrhaphy performed on the left sciatic nerve of injury, removed at secondary neurorrhaphy seven months later. The upper cross section represents the proximal nerve segment, from which the epineurial and perineurial scar tissue and adhesions has been removed. The nerve fascicles are gray, the scar tissue white. Black sutures are seen within the nerve. B, Median longitudinal section through the suture site, with proximal fascicles on right, distal fascicles on left, and suture line fibrosis, sutures, and neuromatous proliferation in mid-segment. Adherent muscle and scar tissue are seen in lower right ( $\times 9.75$ ).

#### *Nerve Suture (Coaptation Suture?) With Débridement; Suture Line Neuroma*

CASE 6 (PNR 218, H. G. H.).—A soldier received a shell fragment wound of the right thigh Oct. 26, 1944. Débridement and primary suture (type not specified) of a completely divided sciatic nerve were done the same day. Re-exploration was carried out May 24, 1945, because of the absence of any clinical evidence of regeneration.

Stimulation after the sciatic nerve had been picked up proximally and distally elicited neither motor nor sensory response. The nerve was then freed from a bed of dense scar tissue and a neuroma in continuity was identified. The lesion was resected and the stumps were cut back serially, a gap of 4 cm. being present when healthy tubules were reached. The branches of the sciatic nerve to the hamstrings and biceps femoris were similarly cut back to healthy tubules because they came off the parent nerve at the point of neuroma formation. Mobilization of the knee joint was difficult because the patient, seven weeks earlier, had had a bone graft of the femur and had been in traction since.

The specimen (Fig. 4) showed a neuroma in continuity. Microscopic examination of the nerve segment, including the site of the initial neurorrhaphy, showed: (1) Proximally, large numbers of regenerating amyelinated neuraves, chiefly in clusters, in tubules which had undergone complete retrograde degeneration and in the proliferated endoneurial network; dense epineurial and interfascicular scar tissue; intrafascicular edema. (2) Medially, foreign body reactions around intraneural silk sutures; at the suture site a fibrous neuromatous reaction in which multiple small regenerated nerve bundles had been compressed by collagenous tissue; degenerative changes in some of these nerve fibers; a thick epineurial "rind" containing necrotic muscle fibers, neuromatous bundles, and scar tissue; penetration of small nerve bundles and individual fibers through scar tissue into degenerated distal fascicles. (3) Distally, small aberrant interfascicular nerve bundles embedded in scar tissue; complete tubular degeneration within the fascicles, with clusters of amyelinated fibers regenerating in old tubules in the proliferated endoneurial fibrous network; intrafascicular edema.

#### *Nerve Suture With Débridement; Massive Wound Infection*

CASE 7 (PNR 247, O. R. G. H.).—A soldier received a rifle bullet wound in the right popliteal space Dec. 4, 1944, with injury of the common peroneal and posterior tibial nerves. Débridement was carried out the following day and both nerves were sutured. The knee was placed in 90 degree flexion. At the end of one week, because of a massive wound infection, the cast was removed, the wound was reopened, and the knee was extended. When there was no evidence of regeneration by May 22, 1945, exploration was carried out, on the indication of the history of infection. A disruption of both neural suture lines was found and several silk sutures were observed in the separated nerve segments.

#### *Nerve Suture With Débridement; Suture Line Neuroma*

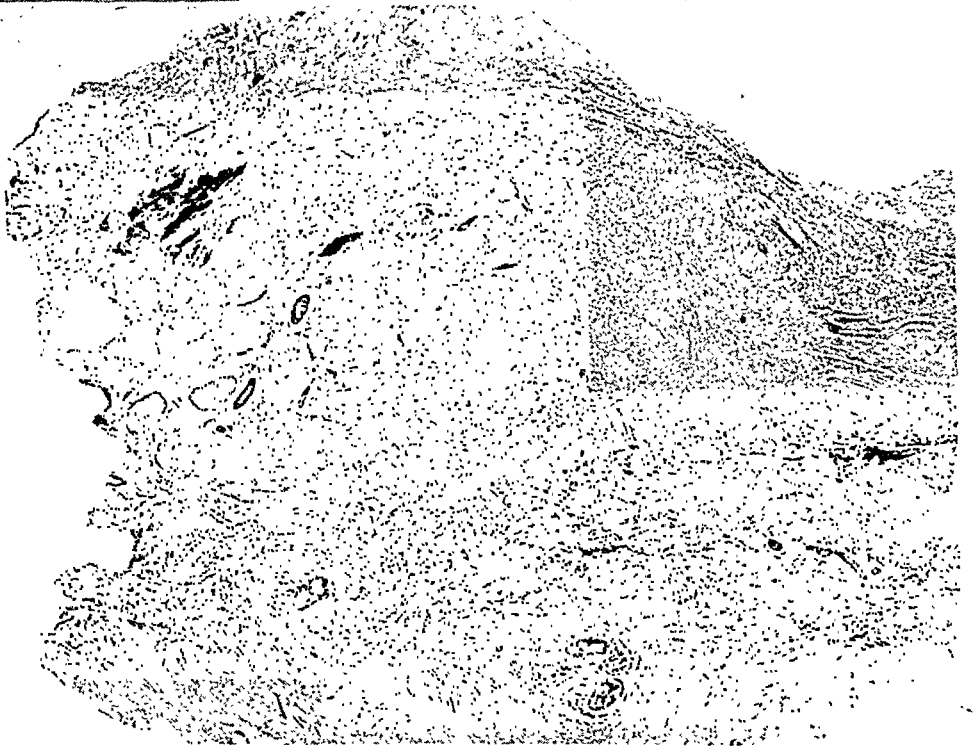
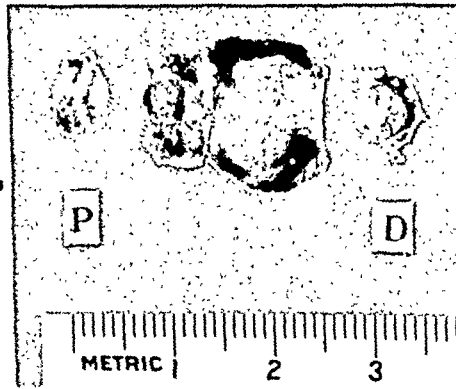
CASE 8 (PNR 126, H. G. H.).—A soldier was injured Jan. 25, 1945, by mortar shell fragments which penetrated the middle third of the right arm. Débridement and suture of the radial nerve with black silk were carried out shortly afterward. A tender mass which developed at the suture site was explored May 19, 1945.

The ends of the radial nerve were identified in scar tissue. Some sensation through the old anastomotic site was elicited on stimulation, but no motor function could be produced. The anastomotic site was swollen and neuromatous, and an occasional black silk suture was visible. Resection of the neuroma left a gap of 3 cm. Moderately satisfactory ends were obtained, although some interfascicular fibrosis was present. The distal end was larger than the proximal, due in part to branching. Secondary nerve suture was performed.

Histologic examination of the segment of nerve at the site of primary suture (Figs. 5 and 6) was reported as follows: (1) Proximally, relatively few lightly myelinated fibers; retrograde degenerative changes in the tubules; numerous fine amyelinated and newly myelinated fibers; moderate intrafascicular fibrosis; marked extrafascicular fibrosis; fusion of fascicles (as noted grossly). (2) Medially, extensive fibrous, neuromatous proliferations; giant cell, lymphoid, and fibrosing reaction in several regions containing silk sutures; heavy scarring and neuromatous formation in the epineurium. (3) Distally, marked intrafascicular and extrafascicular fibrosis; complete tubular degeneration with moderate shrinkage of lumina and replacement fibrosis; numerous very fine amyelinated fibers growing into and between degenerated tubules.

*Comment.*—It is difficult, because of the lack of exact recording of the operation done overseas, to explain the causes of failure in this case except in terms of the pathologic changes found. The presence of a suture line neuroma

A.



B.

FIG. 5 (Case 8).—A, Gross specimen of bulbous suture line neuroma. A trial section has been made to left of main mass. B, Median longitudinal section showing dense mass of neural and collagenous fibers at suture line. Several black silk sutures are seen, not limited to the epineurium ( $\times 10.5$ ).

in a dense mass of scar tissue suggests the possible adverse influence of infection and of compression by the healing muscle wound. The marked fibrosis and the neuromatous reaction at the suture site suggest possible inadequate resection of the damaged nerve segment. The presence of multiple silk sutures within the



neural tissue suggests either poor surgical technique or an alternative pathologic interpretation, namely, that the presumed definitive suture was merely a coaptation suture, for which multiple sutures were used.

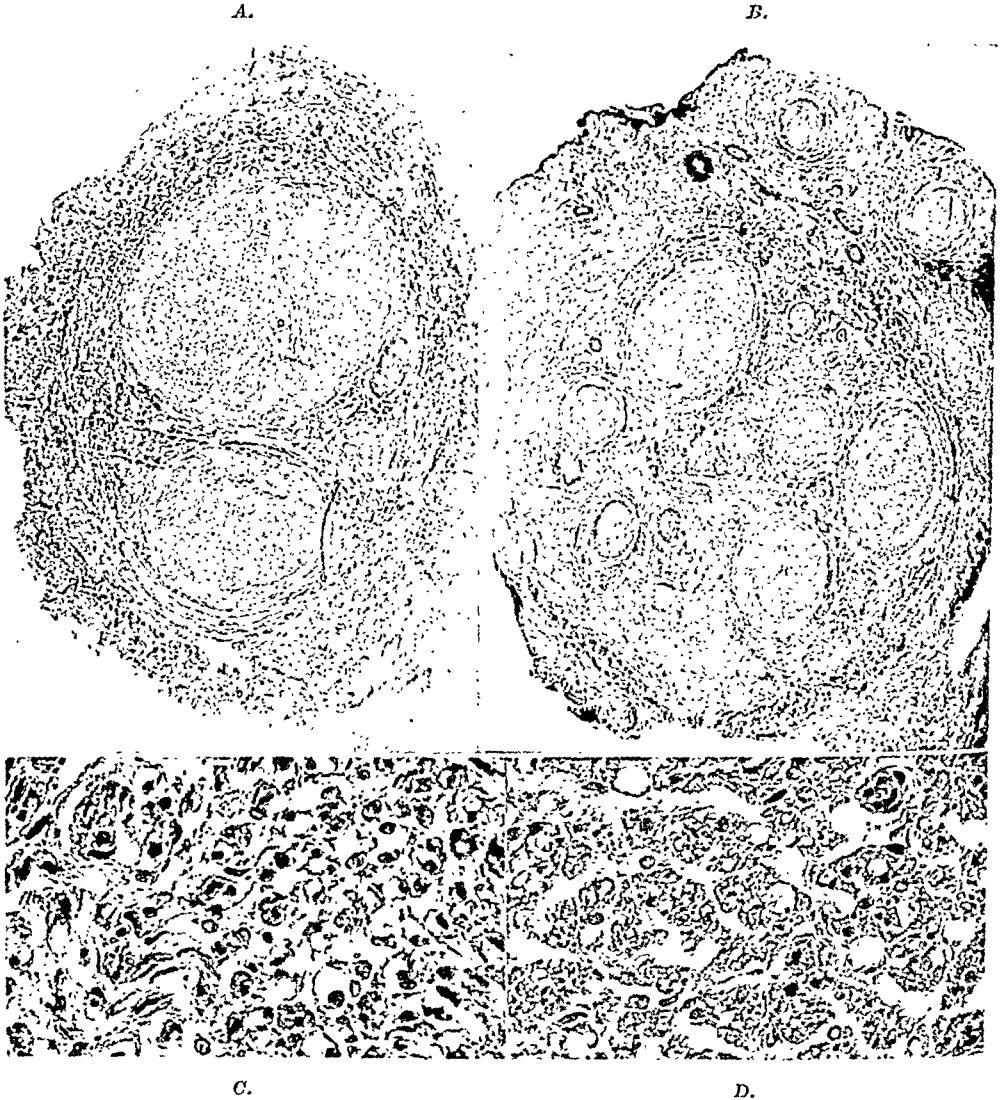


Fig. 6 (Case 8).—A, Proximal stump showing thickened epineurium with moderate perineural fibrosis ( $\times 22.5$ ). B, Distal stump showing many small fascicles, with moderate epineural, perineural, interfascicular, and endoneural fibrosis ( $\times 22.5$ ). C, Proximal stump showing relatively few lightly myelinated fibers and numbers of newly myelinated, expanding fibers. Retrograde degenerative changes have taken place in tubules ( $\times 600$ ). D, Distal stump showing complete tubular degeneration with moderate shrinkage of lumina and replacement fibrosis ( $\times 600$ ).

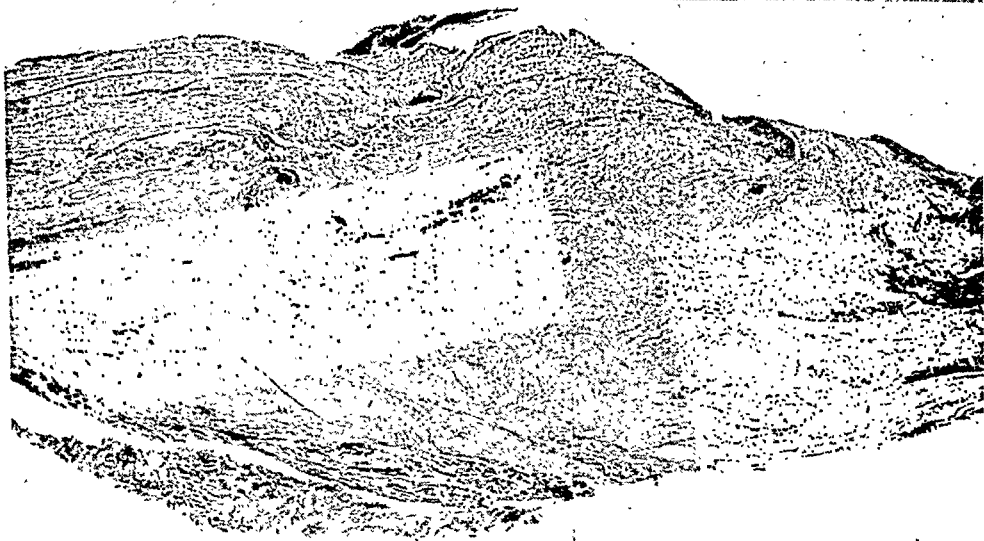
#### *Nerve Suture With Débridement; Suture Line Neuroma*

CASE 9 (PNR 165, H. G. H.).—A soldier sustained multiple rifle bullet wounds of the lower third of the right arm Dec. 31, 1944. Débridement and suture of the ulnar nerve with black silk were carried out the same day. When there was no evidence of regeneration by June 11, 1945, exploration was done.

The incision was carried around the medial epicondyle and into the forearm. Dissection exposed the ulnar nerve as it passes around this epicondyle. The nerve was followed upward into the arm, where it ended in a dense bed of scar tissue about three inches above

the elbow joint. After it had been identified superiorly and freed from the area of scarring, a neuroma in continuity was found. Stimulation above the lesion elicited fair sensory but no motor response. No response of either kind was elicited below the lesion. The flexor carpi ulnaris muscle was then removed from the epicondyle and the nerve was followed downward until the muscular branches in the forearm were exposed. These branches were dissected into the muscle and upward along the nerve until sufficient length for an end-to-end suture was secured. The defect then measured 2.5 cm. The nerve was transplanted in front of the epicondyle and the neuroma was excised; two black silk sutures were found in the center.

A.



B.

Fig. 7 (Case 9).—A, Proximal and distal cross sections and median and external longitudinal sections of anastomotic site; neuroma at suture site. (Higher magnification of the distal cross section in this case showed marked atrophy of the neurolemmal tubules with replacement endoneural fibrosis.) B, Median longitudinal section showing fusiform neuroma in continuity, formed at suture site, and marked foreign body reaction about intraneural sutures ( $\times 10.5$ ).

Histologic examination of the nerve segment at the site of the former neurorrhaphy (Fig. 7) was reported as follows: (1) Proximally, many apparently normal myelinated fibers; nerve tubules in various stages of degeneration and resorption; many amyelinated fibers which had regenerated in old tubules or in the proliferated endoneural fibrous networks; epineural and interfascicular neuromatous bundles in proximal cross section; intrafascicular

edema. (2) Medially, intraneural silk sutures with marked foreign body reaction; dense fibrosis and neuromatous proliferation of nerve fibers from interrupted fascicles; amyelinated neuraxes from the suture line neuroma entering degenerated distal tubules. (3) Distally, degeneration of nerve tubules with resorption of fiber and sheath material and replacement with endoneural fibrous tissue; fine regenerating, amyelinated neuraxes growing into some tubules and into a fibrous meshwork in all fascicles; no recognizable myelination.

*Comment.*—The histologic evidence in this case suggests three important reasons for failure: (1) The silk sutures were badly placed, most of them destroying fascicles directly or giving rise to severe and extensive foreign body reactions which involved other fascicles. (2) The proximal and distal stumps sutured on the day the injury occurred went on to form granulation and scar tissue for some distance from the anastomosis. This process, which cannot be determined within a day of injury, was apparently commensurate with the degree of trauma sustained by the nerve stumps. (3) The neurorrhaphy was performed in a bed which formed adhesions, constricting the nerve and binding it to the surrounding muscle and fascia.

*Nerve Suture With Débridement; Disruption of the Suture Line*

CASE 10 (PNR 207, K. G. H.).—A soldier received a shell fragment wound of the left thigh Nov. 22, 1944. Débridement and suture of the common peroneal nerve were done the following day. Re-exploration was done April 24, 1945, for three reasons: That primary suture of the nerve had been done at débridement, that there had been no descent of Tinel's sign over a period of five months, and that there had been no other evidence of regeneration during this period. Complete disruption of the suture line was found at operation, and re-anastomosis was done.

*Comment.*—In sixteen instances of failure of nerve suture done at the time of débridement the operative record, as in Case 9, was vague or completely lacking in six cases. In the other ten cases the statement was merely made that "suture" or "primary suture" was performed. Pathologic study of the excised anastomotic lines in several cases made it clear that the "suture" mentioned was merely a coaptation suture. The possibilities inherent in such vagueness make clear the importance of describing in detail the method used to repair nerve structures.

The gross and microscopic changes in the anastomotic sites and adjacent nerve segments in these cases demonstrated without much doubt that a coaptation suture, whether intended as such or as a primary suture, holds the nerve trunk in a relatively normal position in the extremity and therefore reduces the degree of resection of pathologic tissue necessary when secondary neurorrhaphy is done. The combination of these factors permitted definitive suture in every instance in this group after routine measures for overcoming the defect had been employed.

In five instances a wound infection of varying degrees of severity clearly played an important role in the destruction of the initial suture line, and also delayed the performance of secondary neurorrhaphy.

In the three cases in this group in which detailed pathologic studies of the anastomotic sites and nerve segments were possible, the time interval between initial injury and definitive suture was, respectively, five, five and one-half, and seven months. In each of these cases the nerve segments exhibited degenerative

changes incompatible with maximal nerve regeneration. As a result of inadequacy of records, the presence of infection, and other causes influencing failure which can only be surmised from a study of individual cases, the average time for final repair in all sixteen cases in which primary nerve suture had been attempted at the time of débridement was 4.9 months. This interval is much longer than it should be, but it can be said fairly that it represents at least a minor triumph for the neurosurgeons who were evaluating this type of case for the first time.

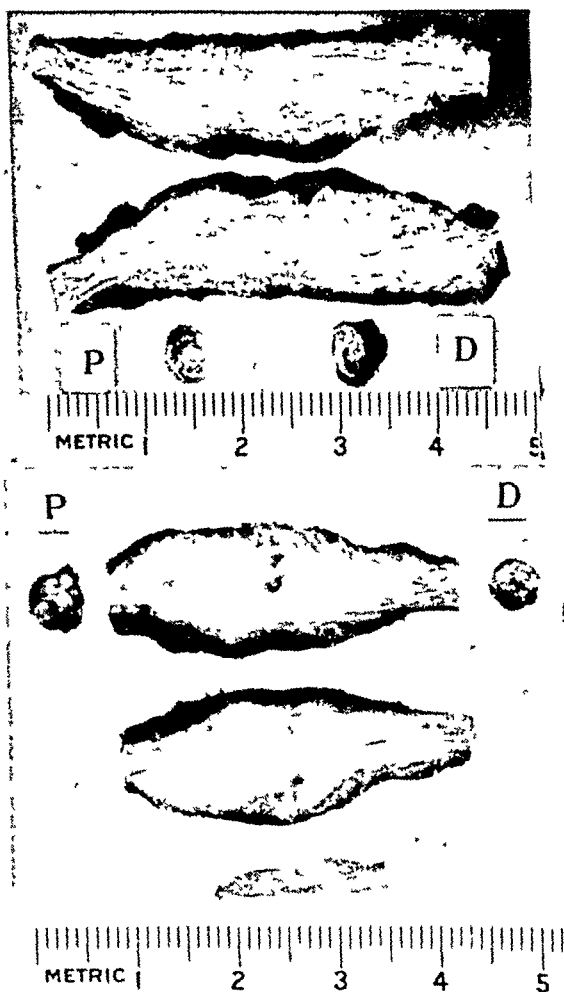


Fig. 8 (Case 9).—Other examples of gross appearance of definitive nerve suture sites in operations performed at time of débridement and removed at secondary neurorrhaphy.

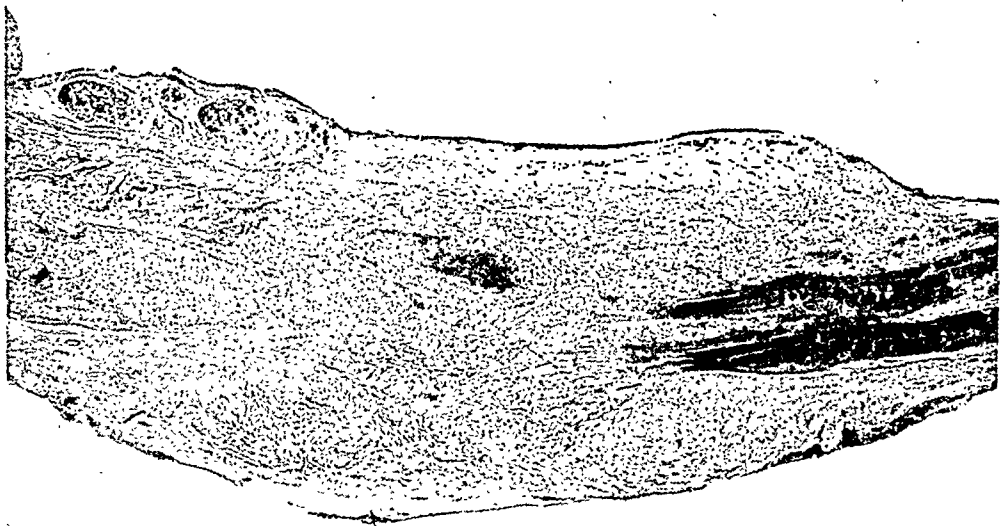
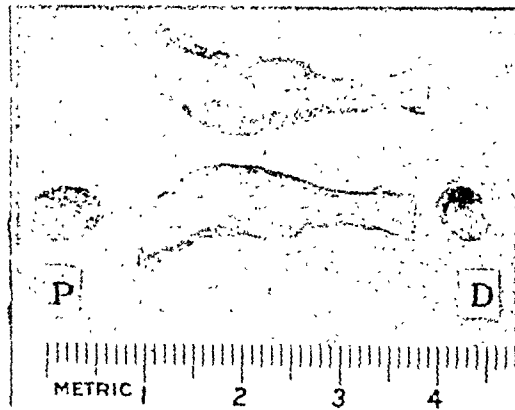
It is interesting to note that the conclusions drawn from this study of coaptation and primary suture at the time of débridement, as well as the relation between total procedures and failures (Table XII), are in strict accord with the experiences of overseas neurosurgeons.

*Coaptation Nerve Suture With Delayed Wound Closure; Definitive Suture One Hundred Five Days After Initial Injury*

CASE 11 (PNR 225, H. G. H.).—A soldier sustained a land mine fragment wound of the left arm Dec. 28, 1944, resulting in a compound, comminuted fracture of the lower third

of the left humerus and immediate paralysis of the left radial nerve. Internal fixation of the fractured humerus, with a wire loop, and delayed wound closure were carried out Jan. 16, 1945. The distal and proximal segments of the injured radial nerve being visualized in the course of the procedure, they were coapted with a single white cotton suture and were surrounded by fibrin film. The operative note was vague as to the details of the procedure (they were secured from subsequent study of the specimen) and for this reason, when no evidence of regeneration had occurred by May 23, 1945, re-exploration was carried out.

A.



B.

Fig. 9 (Case 11).—A, Proximal and distal cross sections and median longitudinal section of radial nerve described as "almost completely severed," which was sutured with a single centrally placed cotton suture and wrapped in fibrin film nineteen days after severance by land mine fragment. Dense scar tissue reaction around white suture in junctional zone and greatly thickened epineurium was observed at secondary neurorrhaphy four months after the first operation. B, Median longitudinal section through suture line neuroma. Note fibrous encapsulation of fibrin film in thickened epineurium at proximal end ( $\times 10.5$ ).

Stimulation of the radial nerve after it had been picked up proximally and distally produced no motor or sensory response. The nerve was freed from an extremely dense scar tissue bed and a neuroma in continuity was identified just above the bifurcation of the radial nerve into its deep and superficial branches. The branches to the brachioradialis and extensor carpi muscles were presumed to have been shot away at the time of injury and to have been replaced by scar tissue; at any rate, they were not visualized. The deep and superficial

branches were traced distally to permit mobilization of the nerve, after which the neuroma was excised and the stumps were cut back serially until reasonably healthy-looking tubules were reached. The gap after surgery was 3.8 cm.

Histologic examination of the segment of nerve containing the suture line (Figs. 9 and 10) showed marked generalized intrafascicular and interfascicular fibrosis; foreign body reactions to suture material and fibrin film; neuromatous proliferation at the junctional zone; proliferating neuraxes choked in endoneural fibrosing reaction in the proximal and distal fascicles.

*Comment.*—It is difficult to determine in this case whether the repair was intended to be definitive. The crude suture technique suggests that it was not,

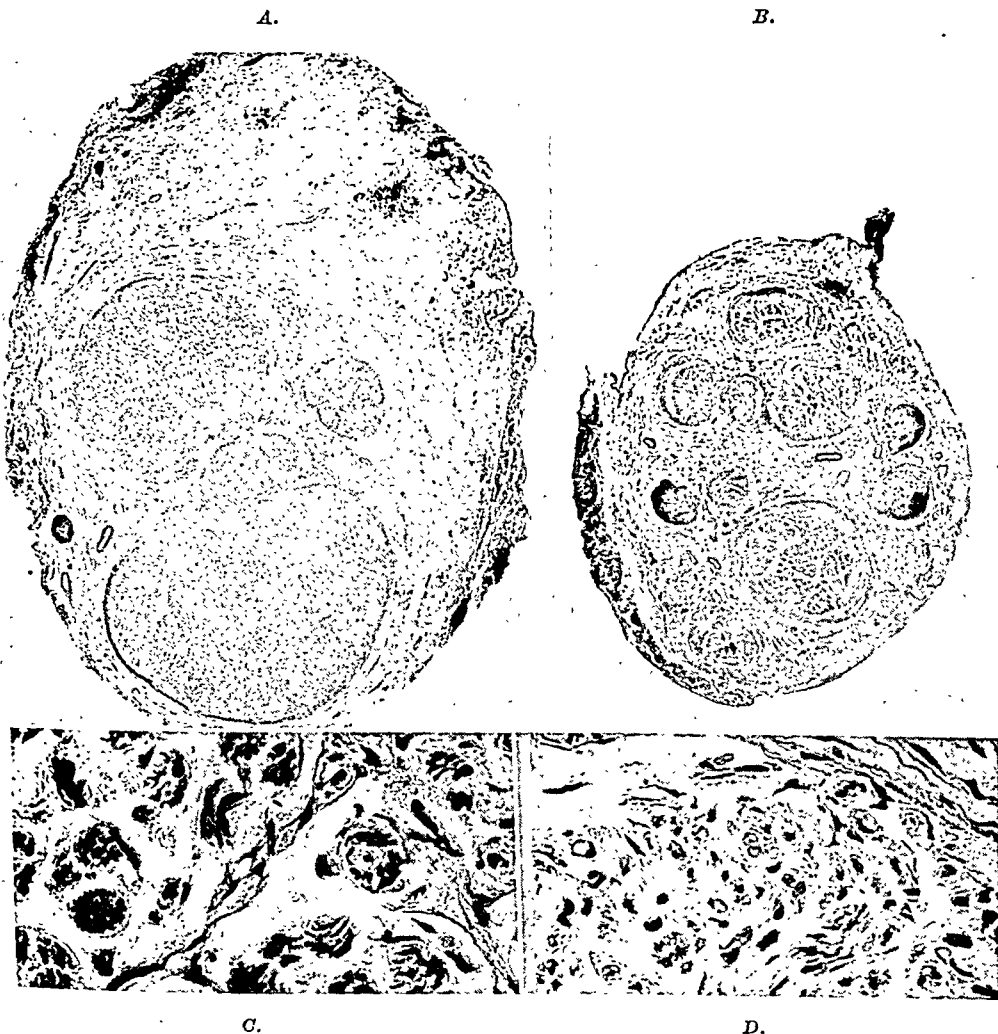


Fig. 10 (Case 11).—A, Proximal cross section representing end sutured at second neurorrhaphy; scar tissue "rind" over epineurium, in which fibrin film remnants appear dark. Most fascicles have become merged in the two large groups ( $\times 22.5$ ). B, Distal cross section representing end sutured at secondary neurorrhaphy. Note generalized fibrosis within and around fascicles, and (dark) fibrin film remnants in epineurial scar tissue and adhesions ( $\times 22.5$ ). C, Cross section of proximal fascicle showing clusters of regenerating branching axis cylinders, many of which occupy old degenerated myelinated tubule. The myelin sheath framework is still present in some cases. Note the group of fine neuraxes around the sheath of a myelinated nerve, and the edema and slight endoneural fibrosis ( $\times 600$ ). D, Cross section through distal fascicle showing fibrotic perineurium, marked endoneural fibrosis, tubular degeneration and shrinkage, and a few regenerated amyelinated neuraxes, some cut tangentially ( $\times 600$ ).

but the wrapping of the nerve, as well as the interval between injury and operation, suggests that it was. The operative record made no mention of resection of the stumps and implied that a connecting strand might have been left between them. On the other hand, the narrow zone of scar tissue separating the proximal and distal fascicles makes it highly probable that the ends were cut back. The insult induced by the sutures and by the dense contracting epineural scar is the obvious, but not necessarily the only, contributory cause in the failure. The possible part played by temporary ischemia, the possible stretch following fracture of the humerus, and the orthopedic manipulations should also be kept in mind.

Secondary neurorrhaphy was amply justified in this case for several reasons, including (1) the complete lack of myelination of the sparsely regenerated distal fibers; (2) the almost total lack of myelination even in the proximal fascicles, in spite of an attempt at regeneration in the midst of endoneural fibrosis; (3) the stationary Tinel sign; and (4) the negative response to direct faradic stimulation when operation was performed.

This case, together with two other similar cases in the series, illustrates failures of definitive nerve suture at the time of delayed wound closure. While the number of favorable results obtained by neurorrhaphy at this time has not yet been determined from analysis of the Registry reports, the indications against it in respect to time are not far removed from those against primary neurorrhaphy with wound débridement. If nerve ends are visualized at delayed wound closure, they should be coapted, but the procedure should end there. The neurologic and operative notes should be written in detail, and eventual solution of the problem should be deferred until wound healing is complete.

*Nerve Suture Forty-seven Days After Injury; Suture Site Neuroma; Minor Error in Tissue Identification*

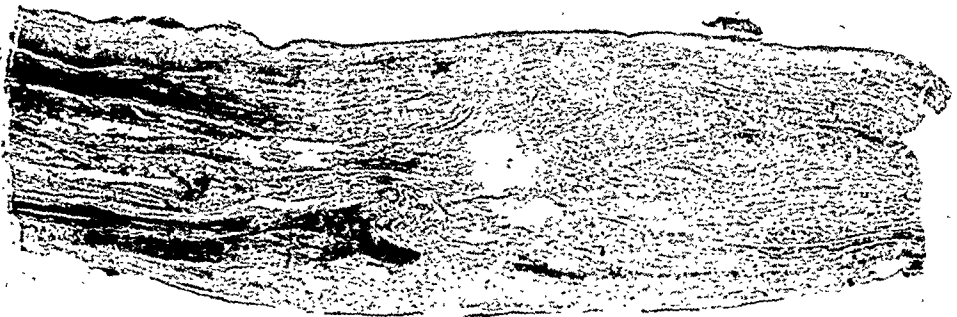
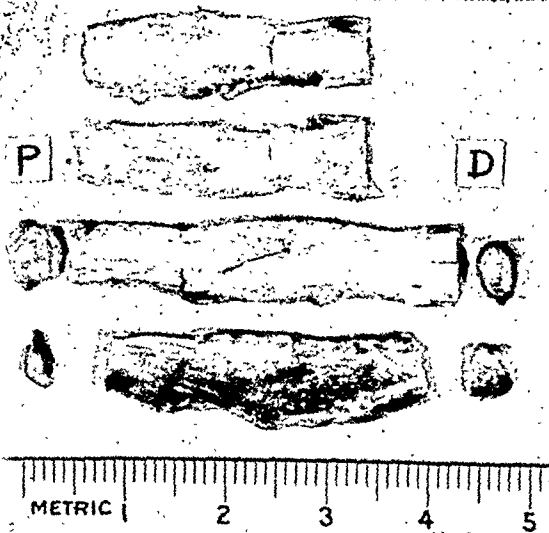
CASE 12 (PNR 50, H.G. II.).—A soldier sustained a shell fragment wound of the popliteal space Dec. 27, 1944. Delayed wound closure was done Feb. 2, 1945, and exploration of the nerve injury was carried out ten days later. According to the operative note, the deep and superficial peroneal nerves were sutured, but the ends of the superficial nerve could not be fully approximated because of a defect, the extent of which was not stated. Re-exploration was carried out April 18, 1945, because there had been no evidence of regeneration.

An incision was made about 15 cm. above the popliteal space. The common peroneal nerve was picked up proximally as it lay medial to the biceps tendon. Stimulation elicited no motor response. The nerve was traced proximally to its point of origin from the sciatic nerve, which was freed up proximally to the proximal point of the incision, and distally to the point at which it had previously been wrapped in tantalum foil. A thin fibroblastic membrane was observed around the foil. The nerve was picked up distally below this level. When the foil was removed, the sural nerve beneath it was found to have been wrapped separately with another cuff of the same material. When this cuff was removed, anastomotic sites in the common peroneal and sural nerves were seen; apparently these nerves had been mistaken by the first operating surgeon for the deep and superficial branches of the common peroneal nerve, for the overseas record stated that these branches had been sutured. The anastomotic sites, which were densely scarred by neuroma formation, were resected and the stumps of the common peroneal nerve were cut back serially until satisfactory tubules were reached, the resulting gap being 4.8 cm. Neurorrhaphy was then done.

Microscopic examination of the anastomotic site (Fig. 11) showed fibrosing reactions around the suture sites; neuromatous proliferation in the proximal and medial segments; random, scanty proliferation of amyelinated neuraxes into distal degenerated tubules; epineural scarring.

*Comment.*—The error in recognition of the point of the main bifurcation of the common peroneal nerve makes it unlikely that the first nerve suture in this case was performed by a trained neurosurgeon. In addition, the biopsy findings were not suggestive of any neurosurgical aptitude. The fine tantalum sutures which should have been placed in the epineurium were found in the neural tissue proper, and the sling stitch (which was obviously unnecessary at the first operation, since it was not required at the second, after resection of

A.



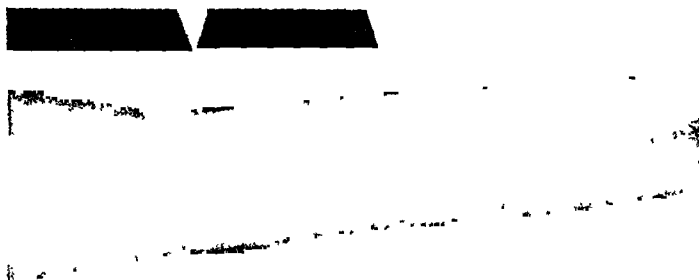
B.

Fig. 11 (Case 12).—A, Proximal and distal cross sections and three longitudinal sections through site of former neurorrhaphy. Upper two sections show 0.003 inch tantalum sutures in fascicles just deep to epineurium. Lower section shows 0.005 inch tantalum sling suture flattened in center of nerve and crossing fascicles obliquely. B, Median longitudinal section through region shown in lower section of A. Proximal fascicles at left end in suture line neuroma and scar tissue around rents made in removing tantalum wire. There is fibrosis of distal end and epineurium has become thickened under tantalum foil ( $\times 8$ ).



approximately 5 cm. of tissue) inflicted serious trauma, and, together with the other misplaced sutures, induced so severe a fibrosing reaction that only negligible regeneration occurred across the scarred anastomosis. The fibers which grew into distal tubules showed no sign of myelination after 3 $\frac{2}{3}$  months.

A.



B.

Fig. 12 (Case 13)—A, Roentgenologic demonstration of suture site in sciatic nerve division, showing wide separation of metallic sutures. B, Disruption of sciatic nerve suture with scar tissue in gap between disrupted nerve ends. (Courtesy of Lawson General Hospital.)

*Nerve Suture Fifty one Days After Injury; Suture Line Disruption*

CASE 13 (PNR 284, L. G. H).—A soldier was injured by shell fragments Jan. 6, 1945, sustaining a sciatic nerve paralysis. End to end anastomosis was done in the mid-thigh Feb. 26, 1945, by means of a stay suture of tantalum (0.005 inch) and epineural sutures of the same material (0.003 inch). The extremity was maintained in flexion only two weeks and extension was developed rapidly. Re exploration was done April 19, 1945, because no evidence of regeneration had occurred and because roentgenologic examination of the suture site disclosed marked distortion of the wire sutures (Fig. 12). A typical suture line disruption, 3 cm. long, was found, and resection of 9 cm. of tissue was necessary before nerve segments free of scar tissue and suitable for secondary nerve suture were reached.

*Nerve Suture Fifty-seven Days After Injury; Suture Line Disruption*

CASE 14 (PNR 33, W. R. G. H.).—A soldier was injured by a penetrating shell fragment June 11, 1944. Following débridement and delayed wound closure, end-to-end anastomosis of the common peroneal nerve was done Aug. 7, 1944, by means of tantalum epineural sutures and a tantalum foil cuff. During the course of evaluation in the Zone of the Interior the patient stated that the knee joint had not been immobilized in plaster following neurorrhaphy. Assessment Oct. 21 and Nov. 23, 1944, revealed no evidence of regeneration, and roentgenologic examination disclosed an apparent separation of the tantalum epineural sutures with loss of the usual orderly outline. Exploration Nov. 23 disclosed a typical suture line disruption, and resection of 6.3 cm. of pathologic tissue was necessary before end-to-end suture could be accomplished.

*Comment.*—The cases cited in this group are typical of the operative findings at re-exploration in sixteen nerve sutures performed at varying intervals after débridement and delayed wound closure. In the group were ten suture line disruptions, five suture line neuromas, and one instance of firm constriction of an anastomosis by a circumferential wire suture. Three of the disruptions were recognized by the presence of a disorganized suture line on roentgenologic examination, and there is little doubt that all might have been diagnosed if this measure had been used routinely.

Unequivocal evidence existed that five of the suture line disruptions were caused by inadequate postoperative immobilization or by failure to immobilize the extremity at all. In two instances disruption occurred in patients in whom the original operating surgeon stated that suture had been accomplished under undue tension. The factors responsible for suture line neuromas are not so clear cut, but it is reasonable to assume that they include tension, postoperative stretch, insufficient resection of pathologic nerve tissue, and poor suture technique.

On the other hand, the small proportion of failures found in the large number of neurorrhaphies performed after delayed wound closure, within the time interval favorable for nerve regeneration, is a tribute to the skill and judgment of the neurosurgeons who cared for these patients. In many of the failures the history of inadequate mobilization suggests that the inadequacy was accidental rather than that there was any deliberate intention of shortening the period of immobilization. Furthermore, suture disruption is a possibility even in favorable cases; the Registry has records of at least two cases in which the accident was recognized while the extremity was still immobilized. Theoretically, maximal strength of the suture site is attained in twenty-one days, but several of these cases suggest that it might be wise to control and maintain immobilization beyond this period.

*Nerve Suture Fifty-one Days After Injury; Premature Unnecessary Re-Exploration*

CASE 15 (PNR 95, N. G. H.).—A soldier was injured by a bomb fragment Nov. 28, 1944, in the upper third of the thigh, with resulting complete sciatic nerve paralysis. Exploration Jan. 18, 1945, disclosed complete division of both nerve components, and end-to-end anastomosis was accomplished with tantalum epineural and stay sutures. When evaluation was carried out in the Zone of the Interior May 3, 1945, the patient volunteered the information that immobilization of the knee joint had been maintained only two weeks. Roentgenologic examination of the suture site revealed no abnormalities, but there was no descent of Tinel's

sign at this time, and re-exploration was therefore carried out March 27, 1945. The suture line was grossly normal and electric stimulation of the distal segment elicited a strong sensory response.

*Failure of Overseas Autogenous Graft, With Slough of Engrafted Tissue;  
Secondary Neurorrhaphy*

CASE 16 (PNR 29, W. R. G. H.).—A soldier received a shell fragment wound of the right arm Oct. 2, 1944. After efforts to decrease the neural defect had failed, an autogenous cable graft 5 cm. long was taken from the lateral femoral cutaneous nerve and was inserted in the ulnar nerve Nov. 16, 1944. When the patient was seen in the Zone of the Interior Dec. 14, 1944, the operative site was tender to palpation. Later the graft sloughed. The draining wound was débrided Feb. 3, 1945, and secondary neurorrhaphy was accomplished March 15 by mobilization, further transplantation, and joint posturing. The defect after surgery was 7.4 cm.

*Nerve Suture Sixty-two Days After Injury; Development of Pseudoneuroma From  
Crumpled Tantalum Foil*

CASE 17 (PNR 140, N. G. H.).—A soldier was accidentally shot in the right forearm July 3, 1944. End-to-end anastomosis was accomplished September 5 by means of epineural tantalum sutures, after which the suture site was wrapped with a cuff of unsutured tantalum foil. Evaluation in the Zone of the Interior April 10, 1945, revealed no clinical evidence of regeneration. A large, tender mass, assumed to be a suture line neuroma, could be palpated at the suture site. Exploration April 16 disclosed a mass of crumpled foil closely adherent to the suture site, which itself appeared fairly normal. Stimulation of the exposed distal segment produced a strong sensory response.

*Nerve Suture Ninety-two Days After Injury; Infection With Protrusion of Tantalum Foil*

CASE 18 (PNR 157, L. G. H.).—A soldier was wounded in the left knee by a mortar shell fragment June 6, 1944. End-to-end anastomosis was accomplished Sept. 6, 1944, by means of epineural tantalum sutures, after which the suture site was wrapped in unsutured tantalum foil. A portion of the suture line over the fibular head was observed to be abraded Oct. 15, 1944, and soon afterward purulent drainage developed and persisted until spontaneous extrusion of the tantalum foil. Healing was then rapid. By March 28, 1945, Tinel's sign had descended 12 cm. and sensory recovery was rated S<sub>2</sub>.

*Comment.*—The eight cases in the group of failures due to miscellaneous causes represent three subsidiary phases of early nerve suture which will be developed in later reports from the Peripheral Nerve Registry. They are of minor importance in the general evaluation of this plan of treatment.

The three instances of nerve grafts in this group are of little value except for the opportunities they offer for academic neuropathologic studies. Since many overseas early nerve sutures in which the suture line was surrounded by a tantalum sheath are regenerating normally, a Registry analysis of such cases at the present time can do little more than state that fact and present variations from the expected progress of regeneration for which, as in the cases cited, the presence of the sheath might be responsible. Case 15 represents the important group of cases, already commented on several times, in which unnecessary secondary exploration must be done in the absence of adequate data concerning previous details of the case.

#### SUMMARY AND CONCLUSIONS

A study of a group of peripheral nerve injuries registered at various times over a twelve-month period in some nineteen separate neurological centers can

indicate at the best only a general trend concerning the value of early nerve suture as a therapeutic method, and the trend can be expressed only in terms of progress toward regeneration or failure of regeneration. A more complete evaluation will be possible as the time interval after operation lengthens and, more particularly, when the regeneration of special nerve injuries is studied. Such analysis are now in progress and will be reported as promptly as possible.

Certain statements, however, may be made at this time and certain conclusions may be drawn from the material analyzed to date. With due regard for the difficulties listed in the maintenance of a peripheral nerve registry, this preliminary survey of the results of early nerve suture indicates that neural regeneration tends to progress satisfactorily after early nerve suture. Both statistical and hand analyses of Registry reports give substantial proof that 85 per cent of the 450 to 649 patients studied over a twelve-month period have demonstrated progressive descent of Tinel's sign and have also shown evidence of motor and sensory recovery. That this problem of military neurosurgery has been brilliantly solved is further proved by the fact that over 90 per cent of the patients received definitive surgery within the favorable three-month period following injury.

While the preliminary statistical analysis of regeneration in nerve injuries over so brief a period of observation is unsatisfactory in so far as end results are concerned, analysis of failures or of variations from the normal course of regeneration is simple. The neurosurgeon responsible for the patient's rehabilitation readily identifies such failures by the employment of certain diagnostic measures and by a study of overseas records for factors which might adversely influence regeneration. His approach to the problem is modified by:

1. The possession of, or the lack of, unequivocal information concerning the type and technique of suture; the presence or absence of previous infection; the extent of postoperative immobilization; the occurrence of postoperative accidents, such as falls or fracture of the cast; and possible ill-considered manipulation of the extremity. The patient submitted to nerve suture overseas and later transferred to the Zone of the Interior arrives under the distinct but unavoidable handicap that there has been a break in the continuity of observation and treatment. Transfer to a new professional environment is facilitated if he is accompanied by detailed neurologic and operative notes concerning his previous course and is handicapped if he arrives without such data.

2. An appreciation of the technical aspects of suture done at the time of débridement or at the time of delayed wound closure as compared with suture done during the later stages of wound healing.

3. The use of all possible diagnostic methods during the period of observation, including roentgenologic observation of the suture line.

4. An attitude of deep suspicion of the clinical course of all patients in whom continuity of treatment has been interrupted by the necessity for evacuation.

The data derived from this preliminary study of the records of the Peripheral Nerve Registry permit certain conclusions which will be of use in the evalua-

tion of early nerve suture if military necessity should again demand its use and which are readily transferred to the civilian practice of neurosurgery. They may be stated as follows:

1. The percentage of failures is far greater when nerve suture is performed at the time of débridement than when it is deferred until after delayed wound closure. The results of this survey and of concomitant pathologic investigations fully substantiate the directives which were issued during the war deerring primary nerve suture and recommending only coaptation or protection of divided nerve ends when initial débridement of the wound was done.

2. While failure of nerve suture done at the time of delayed wound closure has not been found in many cases in the Registry material, it has not yet been possible, either, to identify all the successes which may have followed nerve suture at this time. The evidence now available suggests that primary suture is of dubious value at the time of wound revision and that coaptation suture is the procedure of choice when it is possible.

3. Pathologic studies of cases in which coaptation suture has been done show without much doubt that such a suture, if properly applied, does not increase neural damage at the point of severance or in either segment, while at the same time it prevents retraction of the nerve, which it maintains in its normal anatomic plane. Since the length of the resected coaptation suture site is the only gap to be reckoned with at the time of definitive repair, nerve end retraction having been prevented, whatever technique is appropriate for correcting the defect can be applied readily.

4. Failures in nerve suture performed after delayed wound closure are infrequent and can be traced to two main causes, namely, inept surgical technique and inadequate mobilization, or no immobilization at all, of the extremity after neurorrhaphy. In the forty-four failures studied there were sixteen suture line disruptions, nine of which were directly attributable to improper mobilization of the extremity, and seventeen suture line neuromas, which variously demonstrated the adverse effect of infection, intraneural sutures, tension on the suture line, an unwise selection of suture material, and incomplete resection of pathologic nerve ends.

5. The correction of failures after early nerve suture includes a sound policy of immobilization of the extremity, consonant with function, and the delegation of repair of the injuries to competent neurosurgical personnel. In the latter connection, a small number of errors of tissue identification in this group of failures emphasizes again the importance of concentrating nerve injuries in neurosurgical centers in which they can be cared for by well-trained neurosurgeons.

6. It is not possible to predict the eventual outcome in a contused peripheral nerve visualized at débridement, wound revision, or exploration within the three-month period after injury. Many will progress to neuromas in continuity, which may offer a more or less complete barrier to regeneration.

7. Nerve grafting is still a laboratory procedure except when small nerves, such as the digital or the facial nerve, are involved. It should never be resorted to as a phase of early nerve suture.

8. Detailed operative records and progress notes are essential in all neurosurgical cases. The nature of the injury, particularly of a contused injury for which no operative repair is done, must be described in careful detail. Operative notes must include a clear definition of the type of suture employed in terms of coaptation suture, bulb suture, or primary or definitive suture. Failure to record carefully the details of early operative intervention was responsible in several cases in this study for delay of definitive suture and for a certain number of unnecessary reexplorations. In the absence of such details, evaluation must be based upon a scrupulous search for neurologic changes, which must be weighed against the established expected rate of neural regeneration, the local condition of the suture site, and roentgenologic visualization, which is of great value if metallic epineural sutures have been used. The incidence of secondary explorations is in the last analysis greatly influenced by whether or not the observer is of a suspicious nature. The lack of positive data concerning an earlier procedure is always, in the absence of satisfactory evidence of regeneration, a logical indication for secondary intervention.

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## DECOMPRESSION OF THE ORBIT

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**D**ECOMPRESSION of the orbit is primarily of value for the reduction of severe exophthalmos resulting from endocrine dysfunction. Endocrine exophthalmos is most often seen in Graves' disease, but it may appear along with "spontaneous" myxedema or even without thyroid disturbance. A recent monograph by Woods<sup>1</sup> includes a complete review of the exophthalmos of primary diffuse toxic goiter.

Endocrine exophthalmos apparently results from overproduction of TSH (thyroid stimulating hormone) by the anterior lobe of the pituitary gland.<sup>2-7</sup> An excess of TSH is believed to cause increased water storage in the orbital tissues, with consequent exophthalmos.

There is an apparent exophthalmos in about 65 per cent of patients with untreated Graves' disease,<sup>8-10</sup> and in 4 per cent the exophthalmic symptoms are out of all proportion to hyperthyroid symptoms.<sup>4-6, 11, 12</sup> Subtotal thyroidectomy frequently aggravates exophthalmos in this last group with predominance of ocular symptoms, and may occasionally induce severe exophthalmos even in patients in whom there was none preoperatively. Contrary to general belief, exophthalmos more often increases than decreases after thyroidectomy, the usual apparent recession of the eyes being the result of narrowed palpebral fissures from relaxation of Mueller's lid muscles rather than an actual regression of exophthalmos.<sup>10, 13, 14</sup>

Damage to visual function may result if exophthalmic symptoms become severe. The ocular picture in such cases has been variously termed "malignant exophthalmos,"<sup>15</sup> "exophthalmic ophthalmoplegia,"<sup>16</sup> "progressive exophthalmos after thyroidectomy,"<sup>17</sup> "Graves' disease with disassociation of hyperthyroidism and ophthalmopathy,"<sup>14</sup> and "progressive exophthalmos."<sup>17</sup> Pathologically, in malignant exophthalmos there is an increase in the weight of all orbital structures (muscles, fat, lacrimal gland, etc.) due to increased water storage, with progressive hypertrophy and degeneration of the extraocular muscles, scattered lymphocytic infiltration, and progressive fibrosis of the orbital structures. Clinically, malignant exophthalmos is characterized predominately by increased intraorbital tension or resistance to pressure, by edema of the lids and conjunctiva, and by palsies of the extraocular muscles. Incomplete closure of the lids and impaired nutrition may cause corneal ulceration. The increase in retrobulbar pressure may be great enough to cause papilledema and secondary optic atrophy. Loss of vision has been reported in scores of cases.<sup>17-23</sup>

The acute or progressive stage of malignant exophthalmos usually lasts six months to two years. Lid and conjunctival edema then regresses and, if the eyeball has not been lost, there may be slight to moderate reduction of the exophthalmos. Fibrosis of orbital structures is permanent, with resistance of

the proptosis to manual reduction and some limitation of extraocular muscle function.

Proposed regimes for medical treatment of malignant exophthalmos are numerous and mostly of doubtful efficacy. Administration of thyroid hormone often seems to be of benefit after some weeks or months, and judicious irradiation of the pituitary may be followed by some regression of exophthalmos after two or three months.<sup>24-26</sup> However, during the acute progressive stage of the exophthalmos, visual function is often in imminent danger and treatment must be directed at protection of the visual apparatus itself.

Irradiation of the orbit, resection of chemotic conjunctiva or of orbital fat, and cervical sympathectomy have all been tried, but are usually ineffective. Tarsorrhaphy is of considerable benefit if exposure keratitis develops and if the tarsorrhaphy can be performed without too great pressure on the globe. The most useful form of tarsorrhaphy is an Elshein semipermanent closure of the lateral third of the palpebral fissure. After proper dissection the lateral third of the lower tarsus is sutured beneath the lateral third of the skin of the upper lid. With this procedure firm union practically always occurs, a result rarely obtained in the presence of exophthalmos by simple denuding and suturing of the lid margins. Temporary lid sutures may be used to cover the cornea completely, or the use of ointment and bandage or of a Buller shield may give additional protection to the cornea. However, corneal ulceration may progress in spite of tarsorrhaphy and other protective measures, and tarsorrhaphy itself is of no benefit for pressure atrophy of the optic nerve or for extraocular palsies. Confronted with this not uncommon picture, with imminent danger to visual function, more radical surgical intervention becomes imperative. Some form of orbital decompression is indicated.

It is the purpose of this paper to review the various methods of decompression so far employed, and to discuss an improved technique which has given eminently satisfactory results.

#### HISTORICAL BACKGROUND

Dollinger<sup>27</sup> in 1911 reported a successful lateral decompression of the orbit into the temporal fossa in a patient with Graves' disease and malignant exophthalmos. Marked reduction of the exophthalmos resulted and pre-existing corneal ulceration rapidly healed. Unfortunately, Dollinger's report was overlooked and no other report of orbital decompression appeared until 1931. Tinker<sup>28</sup> in 1912 suggested removal of the lateral orbital wall for malignant exophthalmos, and in discussing his paper Eagleton suggested removal of the orbital roof through a temporal fossa incision, but apparently neither of these men actually performed such an operation. In 1931 Naffziger's first report appeared.<sup>29</sup> He decompressed the orbit into the anterior cranial fossa. His latest report (1938) included thirty-one cases.<sup>30</sup> To Naffziger is due credit not only for devising the transcranial orbital decompression but for teaching the medical profession that orbital decompression can save vision in otherwise hopeless cases. Following Naffziger's first report, interest in the course and treatment of metabolic exophthalmos was greatly stimulated. Semmes (1932)<sup>31</sup>



utilized Naffziger's decompression in one patient. Bothman (1934)<sup>32</sup> tried decompression into the maxillary sinus without effect, and then successfully employed the Naffziger operation on the same patient. Swift (1935)<sup>33</sup> reported a successful lateral decompression. Sewall (1936)<sup>34</sup> described a technique for decompression into the frontal, ethmoidal, and maxillary sinuses, but had performed this operation only on cadavers. Rosenbaum (1937)<sup>35</sup> added another report of a Naffziger decompression. Kistner (1939)<sup>36</sup> successfully utilized the frontal and ethmoidal sinuses for decompression in two patients and described another patient who had a Naffziger operation. Niall (1939)<sup>37</sup> added reports of three more patients operated upon with the Naffziger technique. Spaeth (1939)<sup>37</sup> described a technique of lateral decompression attributed to Shugrue and to Moran; no case reports were published, but in a personal communication Spaeth has summarized the results in five such cases. Guthrie (1941)<sup>38</sup> performed lateral decompressions in one patient. Daily and co-workers<sup>39</sup> (1942) described two decompressions into the frontal and ethmoidal sinuses and a third into the frontal, ethmoidal, and maxillary sinuses. Simpson (1942)<sup>40</sup> performed two other decompressions into the sinuses. Welti and Offret (1942)<sup>41</sup> described successful decompressions in three patients by means of a temporal incision and decompression into both the temporal and the anterior cranial fossae. Savin (1943)<sup>40</sup> added two cases in which Naffziger operations were performed, and Moffatt (1943)<sup>20</sup> and Bardram (1944)<sup>7</sup> each added one. Adler (1944)<sup>42</sup> mentioned one patient who had a lateral decompression of one orbit and a Naffziger decompression of the other, and another patient with an unsuccessful decompression of unstated type. Poppen (1944)<sup>43</sup> described a modification of Naffziger's operation with an analysis of his results in twenty-eight cases.

#### TECHNIQUES AND RESULTS

In its early stages, 1 mm. proptosis results from an increase of 0.75 c.c. of orbital contents. With marked proptosis the ratio decreases to approximately 1 mm. for 1 c.c.<sup>12</sup> Therefore, in decompression of the orbit for marked exophthalmos a reduction of proptosis by 1 mm. should be expected for each 1 c.c. increase in effective orbital volume. However, orbital decompression does not affect the underlying metabolic disorder, and after the retrobulbar pressure is decreased by decompression, still more water storage occurs within the orbit. Thus, the actual reduction of exophthalmos during the acute phase of the disease is not as great as the increase in effective orbital volume would indicate.

The increase in effective volume of the orbit varies directly with the square area of bony orbital wall removed and with the retrobulbar orbital pressure, and inversely with the resistance of the surrounding tissues and with the cohesion or resistance to distortion of the orbital contents. On the whole, the effect of decompression is determined largely by the square area of bone removed (except when the decompression is performed into shallow sinuses, where the inner bony wall of the sinus limits the effect). Also, a small decompression (for example, 4 sq. cm.) has very much more *relative* effect than a large decompression (for example, 10 sq. cm.) because the progressive decrease in retrobulbar

pressure results in less protrusion of orbital contents per square area through the larger opening in the bony wall.

*Decompression Into Anterior Cranial Fossa.*—Naffziger's original operation consisted in removal of as much as possible of the superior orbital plate without opening the frontal or ethmoidal sinuses. He used the usual hypophyseal approach, entering the skull through a frontal bone flap, opening the dura and retracting the frontal lobe, and rongeured off the roof of the orbit along with its dural lining. This resection of orbital roof was extended to the optic foramen and to the superior orbital fissure, and the periorbita (orbital periosteum or orbital fascia) was opened. Later Naffziger found removal of the superior orbital plate alone did not always give sufficient decompression, because in one instance abnormal extension of sinuses into the orbital plate prevented adequate resection of bone. He therefore extended his operation to include resection of the lateral bony wall of the orbit almost to the lateral orbital margin and down to the inferior orbital fissure, thus decompressing the orbit into the temporal or subzygomatic fossa as well as into the anterior cranial fossa.

Poppen employed a slight modification of Naffziger's operation, with decompression of both orbits during the same operation. His technique consisted of a modified coronal incision, bilateral V-shaped frontal bone flaps, extradural exposure by separation of dura from each orbital plate to the sphenoidal ridge (with retraction of the frontal lobe), and removal of most of the superior and lateral orbital walls. In his earlier cases he not only opened the orbital periosteum widely, but divided the fascia through the annulus of Zinn. After producing extraocular palsies in one patient he thereafter obtained equally successful decompressions without opening the annulus of Zinn.

Welti and Offret reported an operation similar in effect to that of Naffziger and of Poppen but with a different approach. They used an incision beginning at the lateral crest of the frontal bone 2 cm. above its external orbital process, extending backward and downward across the temporal fossa. A portion of the insertion of the temporal muscle was cut and retracted. Trephine openings were made (1) through the lateral orbital process of the maxillary bone into the orbit, (2) through the temporal bone at its junction with the great wing of the sphenoid exposing the dura over the temporal lobe of the brain, and (3) through the lateral portion of the frontal bone exposing the dura over the frontal lobe. These three openings were connected and most of the superior and lateral orbital walls removed by means of rongeurs.

The technique of Poppen differs from that of Naffziger in two important aspects: it is bilateral and it is extradural. Operation on both orbits as a single procedure is of undoubted psychologic benefit to the patient, but introduces more physical danger. The extradural approach reduces danger of subdural hemorrhage or of infection, but these advantages are offset by increased trauma in retraction of the frontal lobe when the dura has not been opened and the cisterna magna not evacuated. The technique of Welti and Offret offers the theoretical advantages of an extradural approach with minimal trauma to the brain. However, this technique has been used in only three cases by these

authors, and it is not clear that it gives as good exposure as does the frontal approach.

Most intracranial decompressions of the orbit have included removal of the lateral wall of the orbit and consequent decompression into the temporal fossa as well as into the cranium. However, it is important that the first operations performed by Naffziger, in which only the orbital roof was removed, afforded adequate decompressions. The average area of orbital roof which can be removed in the presence of average-sized sinuses is about 8 to 10 sq. cm. Thus, it seems probable that a decompression of 8 sq. cm. is generally adequate.

To the seventy-four cases of intracranial orbital decompression previously reported may be added four additional cases of Naffziger decompressions performed by Dr. Walter Dandy in the Johns Hopkins Hospital. In the total seventy-eight cases, the decompression was unilateral in twelve and bilateral in most of the remainder. Operation was performed because of actual or imminent loss of vision in fifty-nine cases, because of diplopia in eighteen, and for cosmetic purposes in one.

Four operative deaths occurred. In all fairness to the intracranial technique, it must be recorded that two of these deaths represented attempts of one individual neurosurgeon to utilize the Naffziger operation. In competent hands transcranial removal of the orbital roof is a relatively benign procedure, as evidenced by Dandy's results in removal of orbital tumors by this route.<sup>44</sup>

Three of Poppen's twenty-eight patients exhibited postoperative symptoms of frontal lobe trauma, remaining comatose for periods of four days, two weeks, and four weeks, respectively. All recovered completely.

In the fifty-nine operations performed for actual preservation of vision, success was attained in all but five of the fifty-five patients who lived. Most of these patients had some degree of preoperative corneal ulceration and approximately one-third of them had papilledema with visual field defects. Keratitis and papilledema disappeared and field defects improved. Often very slight reduction in measurable exophthalmos sufficed for preservation of vision—apparently reduction of retrobulbar pressure being as important as reduction of actual exophthalmos.

Improvement of ocular motility was very rapid in some instances. For example, in one of Dr. Dandy's cases measurements of motility before operation and seven days postoperatively showed the following improvement: up, 8° before and 25° after; down, 25° and 45°; in, 15° and 45°; out, 10° and 20°.

Of the eighteen patients in whom diplopia was the presenting symptom, relief of diplopia was attained in thirteen. However, disappearance of diplopia was not always immediate, often occurring several weeks to several months after operation.

The usual sequence of events following operation was as follows: At the completion of operation the exophthalmos showed considerable immediate reduction, with marked decrease in retrobulbar resistance. Within a few hours postoperative reaction caused the exophthalmos to again become marked, occasionally worse than before operation. The postoperative reaction subsided within several days, with a decrease in exophthalmos of 1 to 6 mm. compared with before

operation. Edema of the lids persisted for long periods, often months, but retrobulbar resistance decreased rapidly as the operative reaction subsided. Corneal ulceration was at times aggravated during the stage of postoperative reaction. This could be prevented by lid sutures or tarsorrhaphy and a pressure bandage, and corneal healing proceeded rapidly as the exophthalmos subsided. Papilledema and visual field changes always receded rapidly. Limitation of ocular movements generally improved, often over a period of several weeks or even months. Following the initial improvement in exophthalmos, gradual further reduction usually occurred over a period of months or years. Only rarely after the initial improvement did the exophthalmos again progress, even though the metabolic phase of the disease was still active.

Many patients subjected to intracranial orbital decompression experience annoying pulsation of the globe synchronous with the heartbeat for some weeks or months after operation. This pulsation gradually subsides (Naffziger believed because of the formation of a dense fibrous sheath between orbital and cranial contents) but in one patient described by Kistner reading difficulty continued four years after operation because of the pulsation.

*Decompression Into Sinuses.*—The Sewall operation consists of eradication of the frontal and ethmoid sinuses, through a skin incision, with removal of the orbital walls of these sinuses and of the mucous membrane lining. The roof of the maxillary sinus may also be removed as far laterally as the infraorbital foramen. Orbital contents thus expand into space formerly occupied by these sinuses. Effectiveness of the decompression is dependent on the initial volume of the sinuses. The operation is relatively simple and should not appreciably endanger the patient's life. A theoretical disadvantage of this operation is the possibility of orbital infection, since the operation cannot be performed in an aseptic field. Also, the operation leaves a visible scar.

Results of orbital decompression into the sinuses are available in eight cases. Unilateral decompressions were performed in four and bilateral in four. The operations included the frontal and ethmoid sinuses in six cases, maxillary sinus alone in one, and all three sinuses in one. Operation was performed because of exposure keratitis in five, because of diplopia in two, and for a cosmetic purpose in one.

In one case there was considerable postoperative reaction and it was necessary to reopen the incision two weeks later and drain the wound for one week. In the single patient in whom the roof of the maxillary sinus was removed in addition to eradication of the frontal and ethmoid sinuses, the globe was subsequently displaced downward and there was partial ptosis.

The corneas healed in all five patients operated on for exposure keratitis. In the six in whom restriction of ocular motility was noted before operation, there was improvement of motility in three and no change in three. The exophthalmos receded markedly in five cases (as much as 5 mm. within several weeks in one), appreciably in one, very slightly in one, and none in the single patient in whom only the roof of the antrum was removed.

A comparison of results of decompression into the sinuses with results of intracranial decompression is difficult because of the few reported cases in

the former category. In these few cases the results appear about the same as those in the intracranial operation. The sinus operation has the advantages of being simpler, less dangerous to life, and causing no pulsation of the globes; its disadvantages consist of its dependence on a moderately large frontal sinus for effectiveness, the possibility of orbital infection, and the chance of cosmetic disfigurement.

*Decompression Into Temporal Fossa.*—Dollinger's single lateral decompression of the orbit was performed as follows: A skin incision extended from just above the lateral margin of the brow across the temporal fossa almost to the middle tragus of the ear. The fibers of the temporal muscle were sectioned in the same line and retracted to expose the lateral orbital wall. A wedge-shaped piece of bone was removed from the lateral wall, leaving the orbital margin intact, and the exposed area of periorbital removed. Only the skin was sutured, leaving a gap between the fibers of the temporal muscle.

Swift explored the orbit of a patient with unilateral exophthalmos by the Krönlein route, and when he found no tumor, simply did not replace the lateral bony wall of the orbit. His technique consisted of a horizontal skin incision 7 cm. long extending backward from the external canthus, separation of orbital periosteum from the lateral bony wall, removal of this wedge of bone, and opening of the periorbital.

Spaeth<sup>37</sup> described the technique of Shugrue as follows: A curved skin incision extended from the lateral aspect of the forehead down across the temporal fossa. The temporal muscle was cut and the external orbital wall rongeuired away. Spaeth stated that if more decompression was desired the anterior cranial fossa could also be entered and part of the superior orbital wall removed extradurally—a procedure similar to that of Welti and Offret.

Reports are available of nine cases of decompression into the temporal fossa alone. Unilateral decompressions were performed in five and bilateral in four. Operation was performed because of exposure keratitis in one, because of diplopia in one, because of suspected orbital tumor in one, and for unspecified reasons in the remaining six. There was rapid and marked regression of exophthalmos in eight cases and only transient improvement (2 mm.) in one. In this last case, mentioned briefly by Adler, a Naffziger operation on the other orbit likewise resulted in only 2 mm. reduction of exophthalmos, and the exophthalmos on each side again progressed to its preoperative level within two months after operation. In two of the other patients a lateral decompression was performed on one orbit and a Naffziger decompression on the other; in each instance the improvement of exophthalmos was fully as great with the lateral decompression as with the Naffziger operation.

These few reports allow no conclusions with regard to lateral decompressions except that it appears to be effective and is a benign procedure. The small danger to life from opening the cranium is avoided, pulsation of the globe does not result, and chance of infection encountered with the sinus operation is avoided. However, the techniques previously reported leave a visible scar which may at times be quite disfiguring.

## AN IMPROVED TECHNIQUE

During the past three years eight temporal fossa decompressions of the orbit have been performed on five patients in the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital. The following technique has been evolved.



Fig. 1—A and B, Skin incision 7 cm. long, within hairline.

General anesthesia, usually sodium pentothal, is used. A curved skin incision 7 cm. long, concave forward, is made just within the hairline about 5 cm. back of the superior temporal orbital margin (Fig. 1). This incision does

not extend lower than the middle tragus of the ear. Its exact position is varied in individual patients so the resulting slight scar is entirely covered with hair. The skin is undermined widely up to the lateral orbital margin, care being taken not to incise the fascia overlying the temporal muscle. The lateral orbital margin is then easily exposed by retraction of the skin flap. The periosteum is incised along the entire lateral orbital margin and extending through the fascial insertion of the temporal muscle to about 1 cm. above the superior temporal orbital margin (Fig. 2). The periosteum is then elevated from outside the lateral orbital wall and the temporal muscle retracted into the posterior portion of the temporal fossa (Fig. 3). The lateral edge of the zygomatic process of the maxilla is rongeured away to afford better exposure, and the lateral orbital plate is entered with a craniotomy perforator (Fig. 4). A wedge-shaped section of bone approximately 8 sq. cm. in area is removed from the lateral orbital

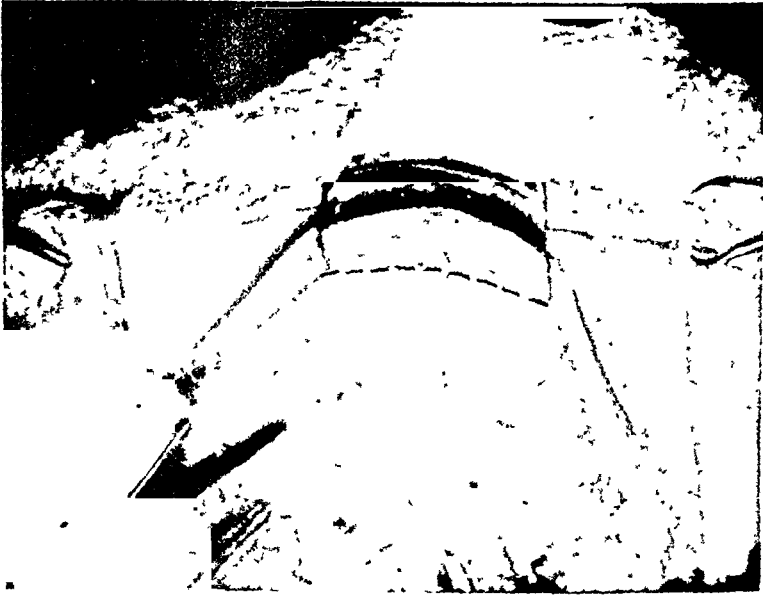


Fig 2.—Incision of periosteum.

wall with rongeurs (Fig. 5). The lateral bony wall is removed anteriorly to within 2 mm. of the lateral orbital margin, inferiorly to the body of the maxilla and the inferior orbital fissure, posteriorly and superiorly to the inner table of the great wing of the sphenoid and to the body of the frontal bone. Care is taken not to injure the infraorbital nerve. Retrobulbar tissue enclosed in orbital periosteum now bulges through the bony opening (Fig. 6). The orbital periosteum is carefully opened with two horizontal incisions parallel to the external rectus muscle, one above and one below the muscle, permitting free protrusion of orbital fat. Trauma to orbital tissues from digital palpation or from biopsy is avoided. Care is taken to control bleeding completely with diathermy coagulation before closure is begun. The anterior edge of the temporal fascia is sewn loosely with silk to the edge of the periosteum along the

orbital margin at one or two points, but avoiding any appreciable pressure of the temporal muscle on the protruding orbital tissue. The skin incision is closed, the lids sutured temporarily (Fig. 7) and a pressure bandage applied over a



Fig. 3.—Exposure of lateral bony wall of orbit.



Fig. 4.—Perforation of lateral wall of orbit.

sponge on the closed eyelids, with only slight pressure over the temporal fossa. If exposure keratitis or marked retraction of the upper lid is present before operation, an Elschnig lateral tarsorrhaphy and insertion of one or two mattress-



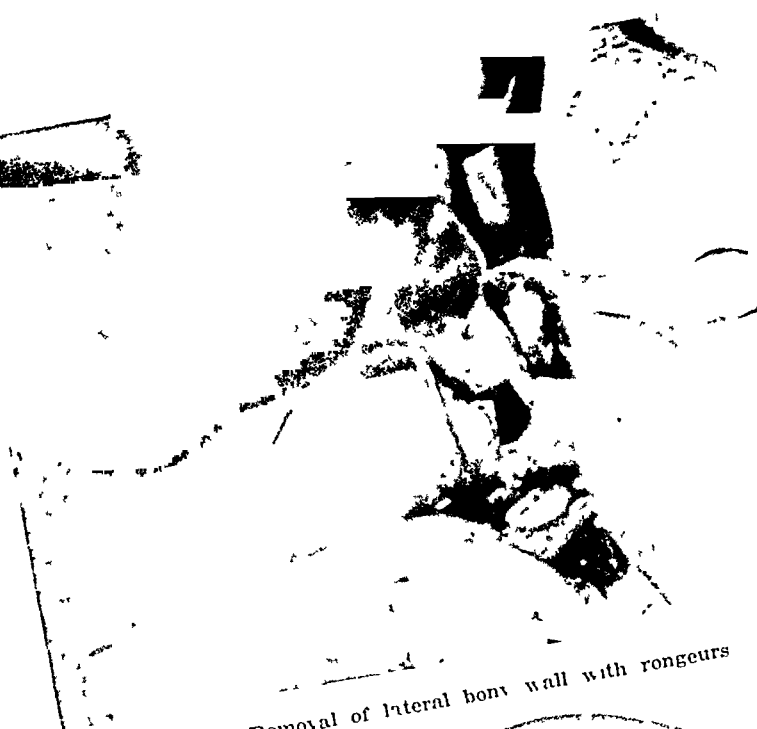


Fig. 5A —Removal of lateral bony wall with rongeurs



Fig. 5B —Diagram of bone removed, anterior view

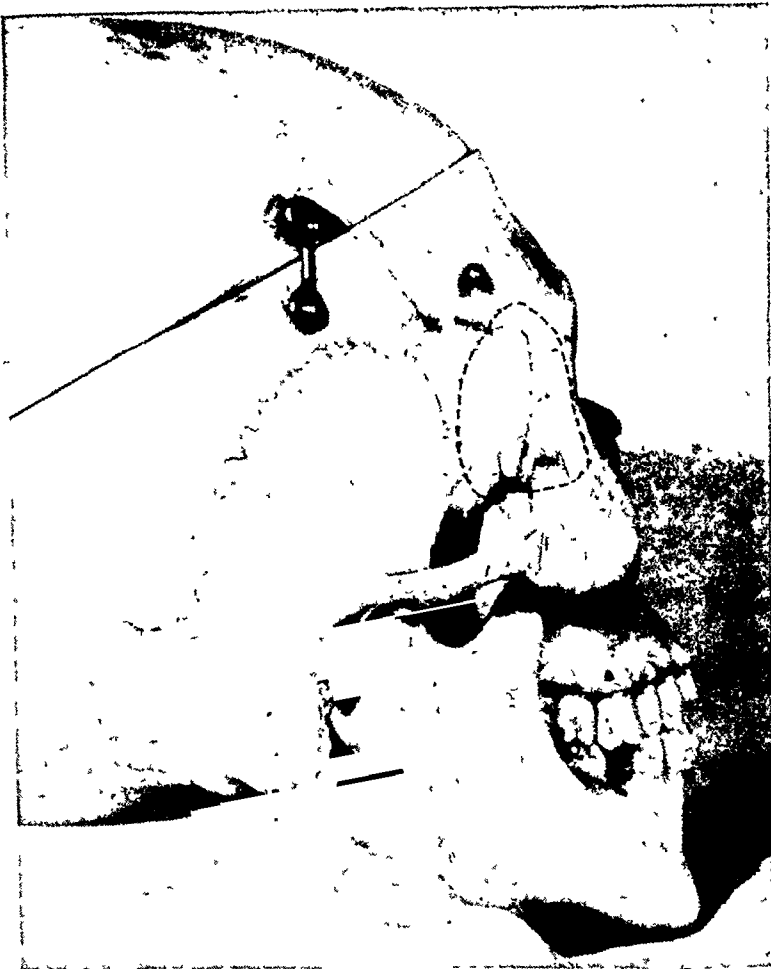


Fig. 5C.—Diagram of bone removed, lateral view.



Fig. 6.—Retrobulbar orbital contents bulging through opening (8 sq. cm.) in lateral bony wall.

type lid sutures is performed before the bandage is applied. The patient is allowed out of bed the following day, and the skin sutures are removed five days postoperatively (Fig. 8).

This procedure gives an entirely adequate decompression. It is performed in an aseptic field and does not endanger any important structures. Postoperative reaction is amazingly slight, some reduction in proptosis generally resulting



Fig. 7.—Closure of skin incision and insertion of temporary lid sutures.



Fig. 8.—Skin sutures removed five days postoperatively.

from the very beginning. Continued reduction in exophthalmos results for several weeks postoperatively, as the slight operative reaction subsides. There is no resulting pulsation of the globe and no visible scar or other cosmetic defect.

Incidentally, a similar skin incision has been used advantageously for removal of a number of orbital tumors through the lateral wall; the visible scar so often apparent after the classical Kronlein<sup>28, 45</sup> operation is thus avoided.

The five patients with lateral orbital decompression operated upon in the Johns Hopkins Hospital showed the following results: In all five patients the exophthalmos receded from 3 to 7 mm. within a period of three weeks after operation. In the two patients with both exposure keratitis and extraocular palsies, the keratitis rapidly healed and the motility improved. In one other patient with diplopia the double vision disappeared within one week. In the two remaining patients operations were performed for cosmetic reasons and because of incomplete closure of the lids. In these patients there was marked cosmetic improvement, and easy closure of the lids resulted. In three of the five patients there was preoperative edema of the lids, which was not reduced by orbital decompression. These five cases are herewith summarized.



Fig. 9 (Case 1).—Preoperative appearance.

#### CASE REPORTS

CASE 1 (No. 280005).—E. F., a white man, was 39 years of age. Fifteen months before lateral decompression of the orbits, the patient developed classical Graves' disease with slight exophthalmos. Eight months after development of symptoms subtotal thyroidectomy controlled the thyrotoxicosis, but three months after thyroidectomy the exophthalmos began progressing in each eye. Just prior to the orbital decompressions the conjunctiva of each

eye showed extreme chemosis and protruded through the palpebral fissures (Fig. 9). There was almost complete immobility of both globes. There was marked exposure keratitis in both eyes. Exophthalmometer readings could not be taken because of the extreme chemosis of the conjunctivae. Basal metabolic rate was  $-15$ . It was impossible to close the right lids manually, but the left could be closed with the patient under general anesthesia. A lateral decompression was performed on the right orbit, together with an extensive tarsorrhaphy, and at the same time a partial tarsorrhaphy was performed on the left lids. There was little postoperative reaction and within one week there was marked regression of right exophthalmos. Ten days after the right orbit was decompressed a similar procedure was performed on the left orbit. Again there was little reaction and the exophthalmos receded rapidly. Reduction of the exophthalmos seemed to be about 5 mm. in each eye within three weeks after the operation and there was partial return of ocular motility. Vision before operation was limited to light perception in each eye, but vision rapidly returned and twenty months later was 20/30 -1 in each eye. Lid edema disappeared very slowly.

CASE 2 (No. 285422) —P. T., a white woman, was 44 years of age. One year prior to the lateral decompression of the orbit, the patient developed classical Graves' disease with moderate exophthalmos. Subtotal thyroidectomy controlled the thyrotoxicosis but six months later the exophthalmos progressed considerably with some edema of the lids and conjunctivae and considerable conjunctival irritation in the left eye. Just prior to the decompression operation there was still marked edema of lids and conjunctiva and exophthalmometer readings were R, 24; L, 26.5. Basal metabolic rate was  $+10$ . The left orbit was decompressed and a small lateral tarsorrhaphy performed at the same time. There was little postoperative reaction. Exophthalmometer readings two weeks after operation were R, 25; L, 22. There was little or no immediate reduction of lid edema.



Fig 10

Fig 10 (Case 3) —Preoperative appearance



Fig 11.

Fig 11 (Case 3) —Appearance twelve days after decompression of left orbit

CASE 3 (No. 331547) —V. L., a white man, was 40 years of age. Ten years before lateral orbital decompression, the patient developed unilateral exophthalmos without signs of thyrotoxicosis. The exophthalmos increased in spite of x-ray therapy of the orbit. An anterior exploration of the orbit revealed nothing and a transcranial exploration through the

orbital roof revealed no tumor and did not improve the exophthalmos, but following this operation there was paralysis of the superior rectus. Six months later the patient developed signs of thyrotoxicosis. This was relieved by subtotal thyroidectomy but the left exophthalmos remained unchanged. The left eye felt continually irritated and eighteen months after thyroidectomy a lateral tarsorrhaphy was performed. In spite of this, recurrent irritation of the left conjunctiva persisted and the patient remained so embarrassed about his appearance that he wore dark glasses constantly during the next eight years. Just preceding lateral decompression of the orbit, exophthalmometer readings were R, 17; L, 23; and there was marked limitation of motion of the left eye on upward gaze (Fig. 10). Lateral decompression of the left orbit and repair of the old lateral tarsorrhaphy caused minimal operative reaction and within twelve days the exophthalmos had receded approximately 3 mm. (Fig. 11). Four months after lateral decompression there was only 2 mm. difference in the prominence of the two eyes. Ocular motility showed no definite increase, but improvement in cosmetic appearance was marked.



Fig. 12 (Case 4).—Preoperative appearance.

CASE 4 (No. 351375).—E. H., a white man, was 40 years of age. Two years before orbital decompressions, the patient developed classical Graves' disease with slight exophthalmos and marked elevation of basal metabolic rate. Subtotal thyroidectomy was performed six months after the symptoms began. Five days after thyroidectomy the exophthalmos rapidly became extreme, with inability to close the eyes and development of exposure keratitis. He received twenty-one x-ray treatments to the orbits, some of these treatments being given with the portal in front of the eyeball. Ten months before the orbits were decompressed the exophthalmos improved slightly and thereafter remained about the same. Just preceding the orbital decompressions exophthalmometer readings were R, 33; L, 35. There was dense scarring of the entire left cornea and of the lower half of the right cornea, with inability to close the lids completely in either eye (Fig. 12). A lateral decompression of the right orbit gave very little operative reaction, with considerable reduction in exophthalmos within two days. Partial tarsorrhaphy of the right lids was performed at the time of operation. Two weeks after the right decompression a similar operation was performed on the left orbit. There was moderate postoperative reaction on this side, with no immediate improvement of exoph-

thalmos. Four weeks after the right decompression and two weeks after the left decompression, there was about 7 mm. recession of the right globe and about 3 mm. recession of the left globe (Fig. 13). The lids were partially closed by tarsorrhaphies and could be completely closed voluntarily without difficulty. Radiation cataract had developed in the right eye and six months after the orbital decompressions this cataract was removed uneventfully. Ocular motility was markedly restricted in both eyes previous to the decompressions, but had improved considerably in all directions when the patient was seen six months later.



Fig. 13 (Case 4).—Appearance four weeks after right decompression and two weeks after left.

CASE 5 (No. 363354).—M. H., a white woman, was 32 years of age. Six months before orbital decompression, the patient developed classical Graves' disease with some exophthalmos and a basal metabolic rate of +67. A subtotal thyroidectomy was performed one month after symptoms developed, but basal metabolic rate remained elevated and the exophthalmos increased slightly, with considerable edema of the lids and conjunctiva. She then received unknown amounts of thyroxin, Lugol's solution, and thiouracil for almost three months. The basal metabolic rate ranged from +15 to +20 with this regime, but there was further slight progression of exophthalmos and two months before the decompression she developed a progressive palsy of the right superior rectus with diplopia in that field. All medication was stopped but the diplopia continued to increase so she could read comfortably only by closing one eye. Immediately preceding decompression of the orbits the basal metabolic rate was +39 and there was almost complete paralysis of the right superior rectus. Lateral decompression of the right orbit caused minimal reaction and both the exophthalmos and superior rectus palsy appeared slightly improved the day following operation. Six days after operation the patient was allowed to use both eyes and was able to read comfortably without diplopia for the first time in almost two months. One week after the right orbit was decompressed a similar procedure was performed on the left orbit, again with very little reaction. Preoperative exophthalmometer readings were R, 21 mm.; L, 20 mm. Three weeks after the first operation exophthalmometer readings were R, 18 mm.; L, 16.5 mm. Quantitative diplopia fields before and after operation showed such marked fluctuation from hour to hour as to be unreliable but appeared to show some average improvement, and the patient no longer had symptoms of diplopia unless she looked up and to the right.

## COMMENT

Orbital decompression is always indicated if exophthalmos progresses to such an extent that there is danger to vision. Thus, it is indicated without question if papilledema or visual field changes appear, or if exposure keratitis develops and the cornea cannot easily be protected by means of lateral tarsorrhaphy.

Use of orbital decompression for diplopia or impaired motility of the globe is subject to some question. Of the eighteen reported cases in which operation was performed primarily for diplopia, the diplopia disappeared in thirteen. However, the diplopia often did not disappear until several weeks to several months after operation and the improvement may in considerable part have represented a remission of the metabolic disorder or gradual readjustment of visual function.

Nevertheless, orbital decompression does at times result in immediate improvement of ocular motility. Some part of the change in extraocular muscles appears to be caused by the increased retrobulbar pressure. From a theoretical standpoint this is in keeping with the observation that increased retrobulbar pressure, induced by the injection of fluid within the orbit, can reduce or even abolish ocular movement.<sup>42</sup> If retrobulbar pressure is reduced by decompression, improvement of ocular motility should occur.

However, no improvement in motility can be expected if the fibers in the involved muscles are completely degenerated and replaced by fibrous tissue, or if fibrosis of the muscle is so extensive as to abolish its elasticity. Thus, little or no improvement can be expected from orbital decompression if the acute stage of orbital edema has already passed.

Decompression can be expected to benefit ocular motility most appreciably if performed just as the muscle palsies are developing. Therefore, decompression appears to be definitely indicated during the early stages of restricted motility in malignant exophthalmos.

Use of the intracranial orbital decompression for cosmetic purposes has been condemned by numerous authors, including Naffziger and Poppen. The appreciable risk to life with the intracranial procedure renders this conclusion sound, but the same objection does not apply to lateral decompression into the temporal fossa. Lateral decompression is a benign procedure and usually results in considerable cosmetic improvement. Marked exophthalmos is generally disfiguring, and often causes considerable embarrassment if not an actual psychosis. I believe lateral decompression for cosmetic improvement is entirely justified provided the patient is willing to undergo a major surgical procedure for this purpose, and provided the patient understands the operation will not relieve lid edema or benefit the underlying metabolic disorder.

Orbital decompression might conceivably be indicated for extreme proptosis from other than an endocrine cause, such as pseudotumor of the orbit, but no such cases have been reported.

## SUMMARY

Orbital decompression will usually preserve visual function in cases of malignant endocrine exophthalmos where other measures fail to halt progression



of ocular symptoms. It is indicated if there is exposure keratitis, papilledema, or early palsy of extraocular muscles.

The orbit can be decompressed into the anterior cranial fossa, the frontal and ethmoidal sinuses, or the temporal fossa. An improved technique utilizing the temporal fossa is described. This operation is the least dangerous of the various decompressions, being extraocular, performed in an aseptic field and not endangering any important structures. It leaves no visible scar or other cosmetic defect and gives a completely adequate decompression. Because of its benign nature, its use is recommended for patients desiring cosmetic improvement of exophthalmic disfigurement as well as for those with threatened impairment of visual function.

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## A METHOD OF ENCEPHALOGRAPHY

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IT IS fitting that an article on encephalography should be included in this tribute to Dr. Walter E. Dandy, both encephalography and ventriculography being due to his clear perception and brilliant initiative. As an indication of the importance of this one of his many scientific contributions, it may be said that the use of gas as a contrast medium for visualization of the intracranial fluid-filled spaces is the most valuable method of neurologic investigation to be introduced since Quinke described lumbar puncture in 1891. It is probable that these methods will never be displaced, for the apparatus is universally available, and the information obtained is based upon definite shadows, which, in most cases, do not lend themselves to individual variations in interpretation.

### INTRODUCTION

Uncertainty as to whether gas will enter the cerebral ventricles is inseparable from the usual methods of encephalography by lumbar injection of gas, and the patient often suffers considerable discomfort. Further, these methods do not always yield the maximum of information. For these reasons an endeavor was made to elaborate a method by which the desired filling could be secured with greater certainty and less discomfort. In order to secure the necessary data, radiography was used to provide a running commentary upon the process of filling. The resulting method was described in *Encephalography*\* and further elaborations were recorded in *Further Contributions to Encephalography*.† Because of dissatisfaction with the original methods, introduction of gas into the cisterna magna has been widely practiced, especially in England and in some European clinics. However, it may be stated that this method lacks the versatility and the reliability of the procedure to be described. By posturing the neck, gas can be delivered with certainty from the lumbar theca into the cisterna magna, or into the subarachnoid space if it is desired. In addition, the freedom of the neck allows certain modifications of posture which may be essential to ventricular filling.

### THEORETICAL CONSIDERATIONS

The method has allowed of an accurate analysis of the influence of posture upon the distribution of air. A series of experiments has shown that the direction taken by the gas along all available pathways, except the ventricular, depends solely upon the physical fact that gas tends to rise through fluid. The entry of gas into the fourth ventricle depends upon filling the cisterna magna. In the sitting patient, flexion of the neck determines the entry of the gas into the cisterna magna, for in the cervical canal the gas travels upward along the

\*Robertson, E. G.: *Encephalography*, Melbourne, 1941, The Macmillan Company.

†Robertson, E. G.: *Further Studies in Encephalography*, Melbourne, 1945, The Macmillan Company.

highest available pathway, that is, dorsal to the spinal cord. There is usually no communication between the dorsal part of the cisterna magna and the remainder of the subarachnoid space over the cerebellum. For this reason further upward passage of gas is possible only through the anterior part of the cistern leading upward to the foramen of Magendie and the fourth ventricle, or by passing at a lower level below the cerebellar tonsils into the subarachnoid space anterior to the medulla and pons. When the patient is seated with his head flexed, the gas rises through the anterior part of the cisterna magna to enter the fourth ventricle. Only when the rate of introduction is rapid, or when the ventricles are replete, does the gas reach the pontine cistern in any quantity by passing below, or sometimes also medial to, the tonsils of the cerebellum. Thus to secure selective ventricular filling it is important to introduce the gas slowly. If the patient's neck is dorsiflexed the gas rises anterior to the cervical spinal cord to enter the subarachnoid space anterior to the medulla and to pass, at higher levels, into the basal cisterns.

That the entry into the ventricles is independent of vital phenomena, such as vascular pulsation, is shown by the fact that gas enters as rapidly in the cadaver, seated with neck slightly flexed, as in the living subject.

That gravitation is responsible for the influence of posture is shown by experiments designed to reverse the influence of flexion and extension of the neck. The gas will enter the fourth ventricle when the neck is extended, and the subarachnoid spaces anterior to the medulla when the neck is flexed, as long as the regions to be filled are uppermost. If the patient lies prone upon an inclined plane, with his head uppermost, the gas enters the cisterna magna and the fourth ventricle when the neck is extended. If the patient lies supine upon the inclined plane, gas enters the pontine and interpeduncular cisterns whether the neck is flexed or extended.

Gas injected into the lumbar theca collects in the dorsal part of the cisterna magna and in the subarachnoid space dorsal to the cervical spinal cord, when the sitting patient's neck is fully flexed. The head may now be dorsiflexed in stages (that is, the flexion is gradually diminished) and roentgenograms taken in each position (Fig. 1). It is found that the gas usually enters the fourth ventricle and the aqueduct when the head is flexed from ninety to eighty degrees. Sometimes the posterior part of the third ventricle is filled at this angle. With further dorsiflexion the third ventricle becomes more and more completely filled, until at about seventy degrees of flexion most of the third ventricle is outlined. Gas usually commences to enter the lateral ventricles when the flexion is reduced to about sixty degrees (Fig. 1). These findings cause surprise, for, in this posture, the interventricular foramen of Monro is considerably below the termination of the aqueduct. Thus, gas passes downward through an originally fluid-filled cavity. This implies that, in this posture, the filling of the lateral ventricles is not due to a direct gravitational effect. An analysis of this phenomenon, its cause and reproduction in vitro, was described in *Further Contributions to Encephalography*. It is beyond the scope of this paper to deal with this point, but it may be stated that the entry of gas into

the lateral ventricles when the head is flexed is due to the disturbance of hydrostatic balance induced by the entry of gas into the lower ventricles. This results in an increase of the pressure in the bubble of gas relative to that of the fluid ahead of it. Expansion of the lateral ventricles allows an inflow of gas to re-establish the equilibrium. As the head is further dorsiflexed, gas

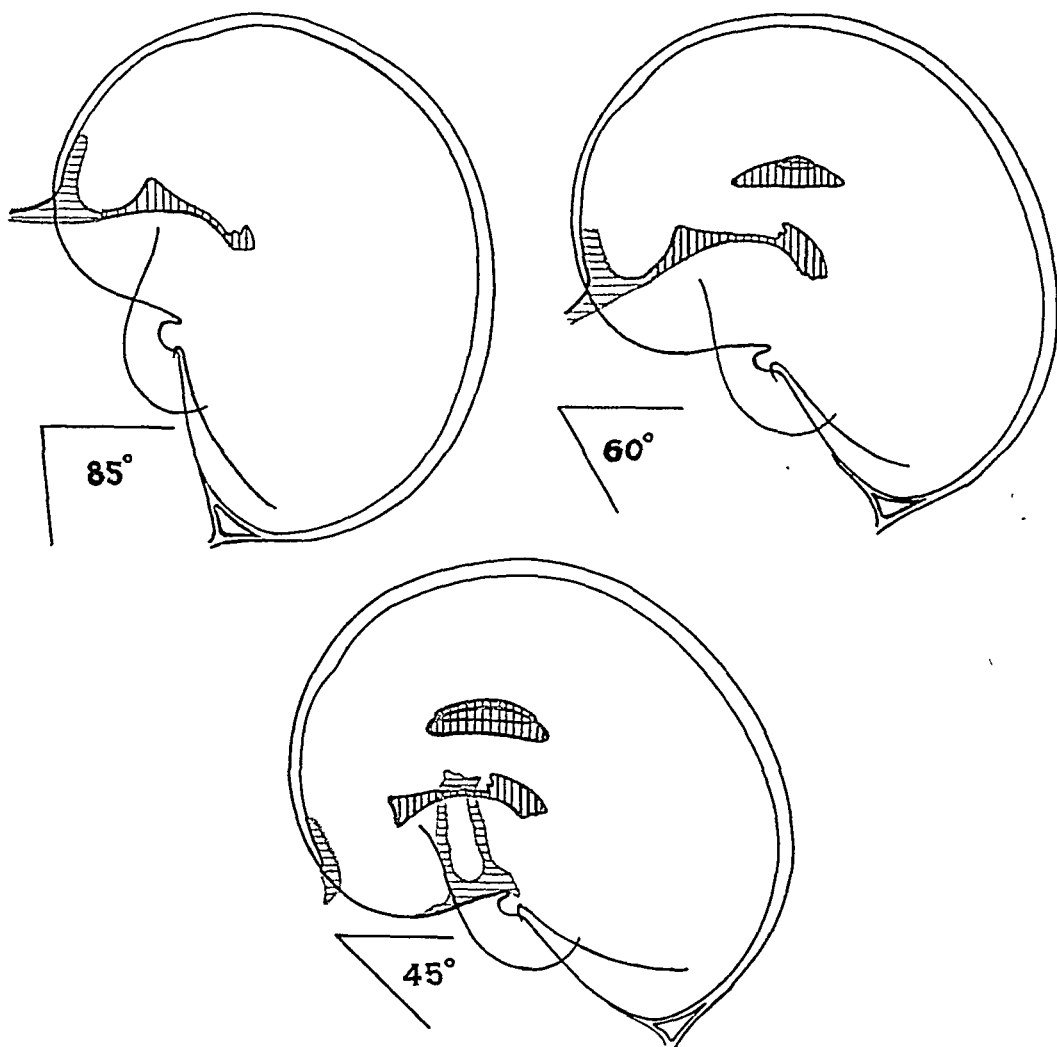


Fig. 1.—Illustrating the influence of posture upon the distribution of gas. Gas is introduced with the head fully flexed, then dorsiflexed in stages. Tracings of roentgenograms taken at eighty-five degrees, sixty degrees, and forty-five degrees are shown. Throughout the illustrations the ventricles are shown in red, subarachnoid cisterns and sulci in green, and cerebral structures, subdural gas, and bones in black.

begins to pass into the pontine and interpeduncular cisterns when the flexion is reduced to about forty-five degrees (Fig. 1). The subarachnoid cisterns, anterior to the pons and medulla, now slope upward and distally. (Under some circumstances this route is followed when the flexion is still greater, as much as sixty

degrees, at which angle the plane of the cisterns is usually approximately horizontal.) At these angles the interventricular foramen is lower than the point of entry of the aqueduct into the third ventricle. The foramen becomes higher only when the angle of flexion is reduced to about twenty degrees. Above this angle the inflow may be determined by direct flotation. The volume of gas in the ventricles increases progressively as the head is dorsiflexed, and is maximal when the head is erect.

#### METHOD

The patient is usually given a sedative before the investigation commences. An injection of omnopon,  $\frac{1}{3}$  gr., followed one hour later by  $\frac{1}{150}$  or  $\frac{1}{100}$  gr. scopolamine hydrobromide has proved very satisfactory for adults. Paraldehyde administered rectally, or ether by inhalation, proves useful for children. During the period of introduction of gas the patient sits in front of the x-ray film. Special chairs may be devised, the essential features of which are the adequate exposure of the patient's back and the provision of ventral support, the latter ensuring that the drowsy or anesthetized patient remains seated in the correct posture. However, special chairs are unnecessary, although in children the procedure is made very much easier by a specially designed support. For adults, the tubular steel chair of modern design or a stenographer's chair with adjustable back is convenient. In these, the patient sits facing the back rest, so that his arms rest upon a cushion fixed to its upper rail. Wide bandages, slung around his back, may be added. The chair is placed so that the patient's forehead rests for additional support against a vertical carrier for x-ray films—usually a Bucky-Potter diaphragm, but even this is not necessary. Firm, gentle fixation of the patient's head is helpful. His chin rests in a depression in an adjustable pad attached to the center of the lower end of the film support. A broad pad of sponge rubber fixed to a curved wooden support eight inches long is connected to the center of the upper end of the table, and is adjusted so that it rests lightly across the patient's vertex. This method allows the taking of posteroanterior and lateral roentgenograms without disturbance of the patient's head. For lateral views a slotted holder for a parallel grid filter and a film cassette is fixed alongside the patient's head, at right angles to the Bucky-Potter diaphragm. By adjustment of these supports the patient's back and neck are flexed to the desired angle. When it is desired to fill the cerebral ventricles the head is flexed to about thirty degrees.

Two lumbar puncture needles are introduced, using local anesthesia, into neighboring lumbar interspinous spaces. The type of needle provided with two outlets controlled by a three-way tap, such as that designed by Greenfield, is most convenient. A length of glass tubing (70 cm.) of 2 mm. bore is attached to one outlet of the lower needle, thus providing for measurement of pressure (Fig. 2). When the pressure is normal, the cerebrospinal fluid rises to about the horizontal level of the foramen magnum. A syringe of 20 c.c. capacity is filled with oxygen from a cylinder of the compressed gas, by means of a sterilized rubber tube, in which is incorporated a cotton-wool filter. Gas is then slowly injected through the upper needle, while fluid is allowed to drip from lower needle at such a rate

the manometer. When 7 c.c. of gas have been injected, a posteroanterior or lateral roentgenogram is taken with the center ray directed horizontally. The film is developed and studied as soon as it is available. The component parts of the shadow are readily recognized in lateral views. The tracing of a typical posteroanterior roentgenogram is shown in Fig. 3, *a*. When the central ray

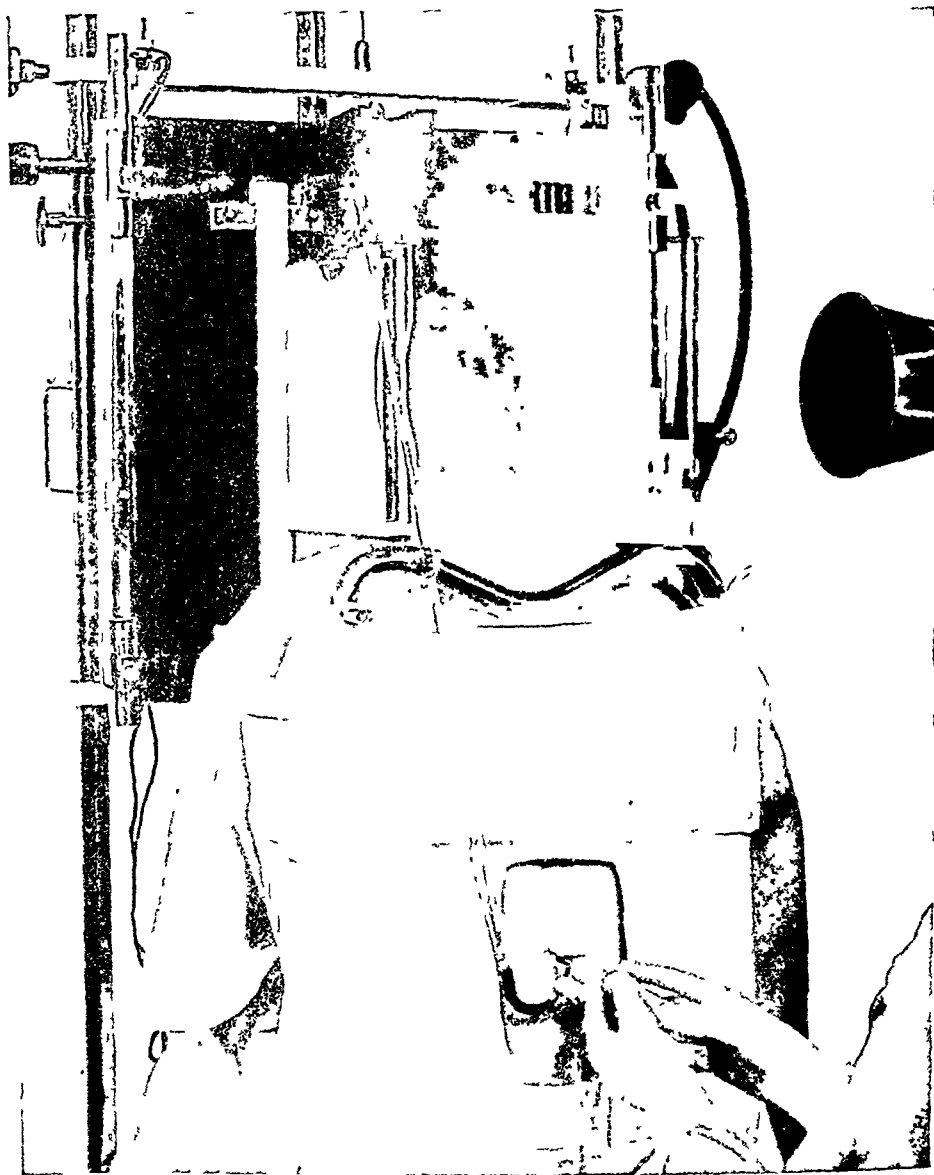


Fig. 2.—Showing the general arrangement a lateral roentgenogram is being taken.

makes an angle of about thirty degrees with the long axis of the skull (which corresponds to the horizontal plane when the head is erect) the shadow of the fourth ventricle has a somewhat rounded appearance (*F*, Fig. 3). The aqueduct inclines forward, away from the x-ray tube, and its distal part is actually

along the line of the rays. Hence, the upper part of the aqueduct is shown as a dense round shadow (*D*). The inclination of the head causes the lower part of the shadow of the third ventricle (*C*) to overlap that of the fourth ventricle. A narrow column is seen in the midline below the fourth ventricle (*G*). This is due to gas in that part of the cisterna magna between the tonsils of the cerebellum (with the medulla in front and the vermis behind\*) and in the lower part of the fourth ventricle, between the two vertical limbs of the choroidal plexus. The component shadows are clearly seen when the head is slightly rotated (Fig. 3, *b*). Other appearances in the first films, which may indicate the necessity of modification of technique in order to obtain satisfactory filling, are dealt with in a subsequent section. If the film is satisfactory, the interchange of gas and fluid is continued until an adequate filling is seen. Usually about 20 to 25 c.c. suffice to outline the ventricles. If filling is continued after

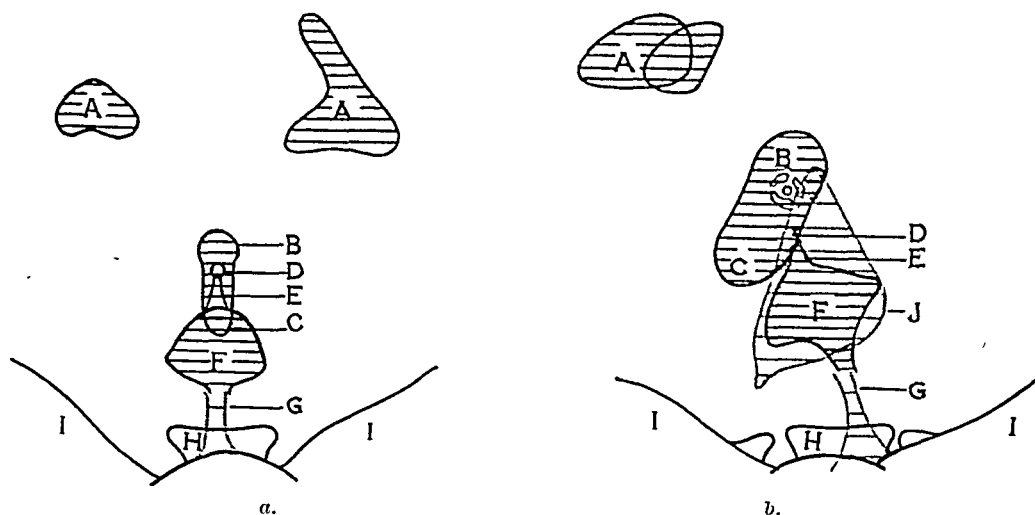


Fig. 3.—Tracings of posteroanterior roentgenograms, the head being flexed thirty degrees and the central ray horizontal. (*a*) A typical film; (*b*) The ventricles dilated and the head slightly rotated. *A*, lateral ventricles; *B*, suprapineal recess; *C*, body of third ventricle; *D*, *E*, aqueduct of Sylvius; *F*, fourth ventricle; *G*, anterior part of cisterna magna leading to foramen of Magendie; *H*, dorsum sellae; *I*, petrous temporal bone; *J*, posterior part of cisterna magna.

the ventricles are replete, the gas passes into the pontine and interpeduncular cisterns, and thence into other parts of the subarachnoid space. Hence, a complete filling may be secured without disturbing the position of the head. However, certain cisterns, or chosen regions of the subarachnoid spaces, may be demonstrated by the use of small volumes of gas, directed by posture to the region under consideration. If the head is flexed the gas passes along the ambient cisterns to their confluence in the cisterna venae magnae cerebri. Then it passes into the dorsal part of the callosal sulcus, the occipitoparietal and calcarine fissures, and the sulci over the convexity of the occipital lobes. If the head is extended, the gas passes forward into the chiasmatic cistern, the

\*In accord with common usage, the term cisterna magna is used to describe that part of the cistern posterior to the medulla. For convenience of description, this is subdivided into a small anterior part, described above, and a larger posterior part superficial to the inferior surface of the cerebellum. As first described, the cisterna magna also included the subarachnoid space anterior to the medulla. This part the author differentiates as the medullary cistern.



cisterna laminae cinereae terminalis, the Sylvian fissure and into sulci on the medial and lateral surfaces of the frontal and parietal lobes. If the head is erect both routes may be followed. If the head is inclined to one side the gas will pass into the subarachnoid space over the uppermost hemisphere.

When a roentgenogram shows that the region under consideration has been demonstrated effectively the needles are removed and the patient placed in a recumbent position, with his forehead uppermost. An injection of morphine may be given at this stage to reduce the headache which occurs when the head is moved. The following sequence of postures proves satisfactory for radiography in the recumbent posture. The head is rocked from side to side to equalize the distribution of gas and an anteroposterior roentgenogram is taken. If the lesion is believed to lie in the anterior parts of the third or lateral ventricles a lateral view may be taken in this posture. This view is particularly useful when gas has also been introduced into the chiasmatic cistern. Next the patient lies prone and a posteroanterior view is taken. He then lies on one side during a period of some three minutes in which the head is manipulated to secure the passage of as much gas as possible into the upper lateral ventricle. Stereoscopic lateral films are taken. An anteroposterior view with the head in the lateral posture is useful in demonstrating the cross section of the temporal horn. The shadow is best seen when it falls between the petrous temporal bone and the lesser wing of the sphenoid. The central ray, passing along the sagittal plane of the skull, makes an angle of about twenty degrees with a line between the outer canthus of the eye and the external auditory meatus. Finally the patient lies on his other side while the gas is transferred to the other ventricle. Similar views of this ventricle are taken. The views are studied before the patient returns to bed so that any necessary amplification can be obtained by repetition, or the taking of supplementary views.

The whole procedure occupies about sixty minutes. There is little reaction to the usual procedure. Some 500 patients have been examined by this method, using two needles to maintain constancy of pressure. It is believed that this factor deserves stressing, for no untoward reactions have been observed, although over sixty neoplasms are included in the series. Some of these were in the cerebral hemispheres (a number producing gross ventricular displacement), some were suprasellar in position, and some were in the posterior fossa. When the lumbar pressure is much elevated, or if there is evidence of incisural or foraminal herniation, ventriculography is used instead of encephalography if evidence of localization is necessary.

As an example of the use of small quantities of gas to demonstrate special regions, the visualization of the suprasellar region may be described. The lateral ventricles and the third ventricle are filled with the head flexed to thirty degrees, and a lateral roentgenogram is taken. The head is then dorsiflexed (about ten degrees behind the erect posture) and filling is continued. The gas now rises into the interpeduncular and chiasmatic cisterns. Lateral and posteroanterior views are taken. If the filling of ventricle and cistern is satisfactory the patient is placed in recumbency and a lateral roentgenogram is taken with the brow up. This shows the anterior part of the lateral ventricles, the third

ventricle with its chiasmatic and infundibular recesses, the related cisterna chiasmatis, cisterna interpeduncularis, and lamina terminalis.

#### CAUSES OF FAILURE AND RECTIFICATION

The first roentgenogram taken in the erect posture may fail to show the fourth ventricle. There are a number of reasons for this, some of which suggest the necessity of modification of technique if ventricular filling is to be achieved.

*Large Cisterna Magna.*—The cisterna magna varies greatly in capacity. If it is unusually large, many cubic centimeters of gas may be expended in filling its dorsal part before gas enters the ventricles. Usually the posterior part is small, extending about 3 cm. behind the foramen magnum, and reaching to within 2 or 3 cm. of the inion. In such cases, the fourth ventricle will be outlined in the first roentgenogram. When the cistern is large it is seen in lateral views following the curve of the inner surface of the occipital bone as high as the internal occipital protuberance (Fig. 4, *a*). In posteroanterior views the cistern is represented by single or paired shadows, one on each side of the midline of the posterior fossa (Fig. 4, *b*). As the quantity of gas increases the shadow extends down toward the foramen magnum, and eventually, in posteroanterior views, a denser narrow shadow appears in the midline above the foramen (Fig. 4, *b*). The appearance of this column precedes filling of the fourth ventricle. It represents the anterior part of the cistern, just described, from the apex of which the foramen of Magendie gives access to the fourth ventricle. If the ventricle does not contain gas, and a large cistern is seen, a further introduction will probably lead to ventricular filling. The posterior part of the cistern has usually to be filled before gas enters the fourth ventricle, although some gas may rise directly into the ventricle through the anterior part of the cistern, especially if the head is erect. The gas in the posterior part of the cistern may be made to flow into the fourth ventricle by dorsiflexing the head. This brings the posterior part of the cistern to a lower level than the anterior part, and the gas rises through the latter into the fourth ventricle. In some cases the patient may be conscious of the gas bubbling within his skull. The transit is rapid and is usually accompanied by the development of frontal headache. The same transfer of gas is produced by lowering the patient slowly from a sitting to a recumbent posture at the end of filling.

*Passage Into Ventral Cisterns.*—In lateral roentgenograms the gas may sometimes be seen in the pontine, interpeduncular, and ambient cisterns, having failed to enter the ventricles (Fig. 5, *a*). In posteroanterior views the gas is seen in the ambient cisterns (Fig. 5, *b*) which may be recognized as an arched shadow, the two anterior pillars arising on each side from the interpeduncular cistern (the shadow of which overlies and rises above the dorsum sellae) and converging above and dorsally in the cisterna venae magnae cerebri, which in this view is situated about 3.5 cm. higher than the shadow of the dorsum sellae. In some cases the ambient cisterns appear to receive gas from collections seen, in this view, above the shadows of the medial parts of the petrous temporal bones. These collections are in the upper part of the lateral recesses of the pontine

cistern underneath the tentorium. Laterally the gas is situated below the attachment of the tentorium to the petrous temporal bone. More medially, the gas passes dorsally below the inferior surface of the tentorium, and then around the midbrain in the lower part of the ambient cistern to reach the cisterna venae magnae cerebri.

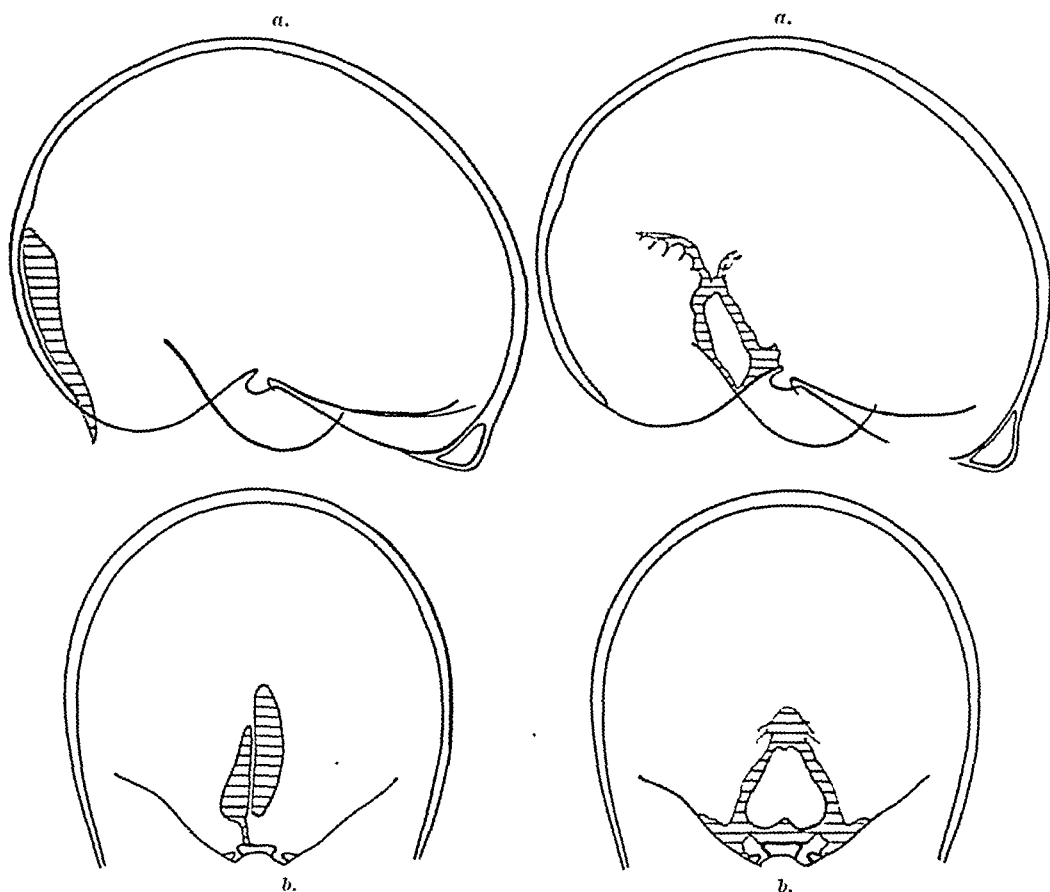


Fig. 4.

Fig. 5.

Fig. 4.—Tracings of lateral and posteroanterior films showing large cisterna magna.

Fig. 5.—Gas in pontine, interpeduncular, and ambient cisterns. In the lateral view gas is also seen over the superior surface of the cerebellum.

This passage of gas into the ventral cisterns is the commonest cause of initial failure of ventricular filling. In these cases ventricular filling may be secured by introducing the gas with the neck more fully flexed, and then slowly dorsiflexing the head. The pronounced flexion determines the passage of the gas into the cisterna magna, where it accumulates. When the head and neck are dorsiflexed after each introduction the gas passes into the fourth ventricle. This results in filling in all but a very small percentage. Indeed, if failure results it is almost certain that some form of pathologic obstruction exists. This method of filling in full flexion followed by dorsiflexion is an excellent

routine procedure, since it decreases the percentage of failures. It is to be recommended if roentgenograms are not taken during filling, or if time is limited. The only disadvantage is that the procedure becomes more trying to the conscious patient, for he complains of frontal headache during dorsiflexion.

*Escape From Cisterna Magna.*—In a small percentage of cases (about 2 per cent) the gas reaches the cisterna venae magnae cerebri without passing along the pontine, interpeduncular, and ambient cisterns (Fig. 6). The roentgenograms show that gas escapes from the apex of the cisterna magna, which in

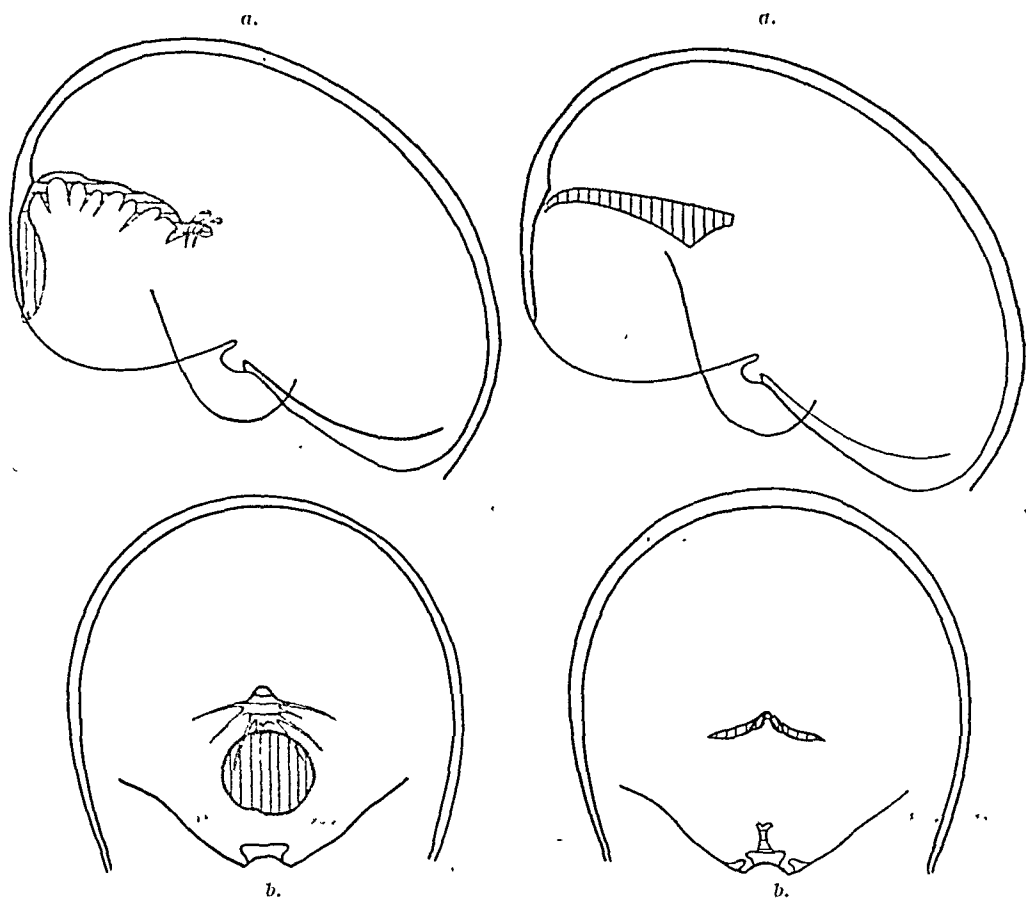


Fig. 6.

Fig. 7.

Fig. 6.—Gas reaches the cisterna venae magnae cerebri by passing over the surface of the cerebellum. In the posteroanterior view the cisterna venae magnae cerebri (hatched horizontally) is seen above the large cisterna magna (hatched vertically).

Fig. 7.—Gas in the subdural space under the tentorium. The posteroanterior roentgenogram was taken after 5 c.c. had been injected, the lateral after 10 c.c.

these cases is not sealed off from the remainder of the subarachnoid space over the convexity of the cerebellum. The gas which enters the dorsal part of the cisterna magna flows over the surface of the cerebellum to reach the cisterna venae magnae cerebri. If the aperture transmits gas rapidly, the ventricles will not fill until the dorsally placed subarachnoid spaces are replete. If the head is placed in the erect posture, however, some gas will rise directly into the

anterior part of the cistern and thence into the ventricles. In this way, coincident filling of the ventricles and the dorsal cerebellar subarachnoid space is produced.

*Subdural Insufflation.*—In some instances a large shadow of somewhat triangular shape, is seen in lateral views (Fig. 7, *a*). The base extends forward from the region of the internal occipital protuberance and the apex is situated anteriorly at a considerably higher level. Should the ventricles also fill, the apex will be seen to lie near the position of the splenium of the corpus callosum. The gas outlines the undersurface of the tentorium. In posteroanterior views a narrow column can be distinguished for varying distances above the foramen magnum, the distance depending chiefly upon the rate of introduction (Fig. 7, *b*). As more gas is injected a transverse shadow with a denser central peak appears at a higher level, due to gas collecting underneath the tentorium. After passing through the incisura tentorii, the gas outlines each side of the falx and superior longitudinal sinus and collects over the convexity of the cerebral hemispheres. In such cases the gas has been introduced into the subdural space. The use of a sharp fine needle with a short bevel makes this occurrence less likely. A long bevel may lie in both the subarachnoid and subdural spaces. In other instances the bevel slips from the subarachnoid space, in which it originally lay, into the subdural space. Fluid escapes through the puncture in the arachnoid and is evacuated through the needle. This escape allows the relative collapse of the arachnoidal sac, so that it may be difficult to pierce the arachnoid again. Under these conditions it is best to withdraw the needle and insert it into a neighboring intervertebral space. Even this may fail in securing its object, and it is then necessary to resort to cisternal puncture.

In rare instances it is impossible to fill the ventricles by any maneuver. Occlusion of the foramen of Magendie may be responsible, but in adults the presence of a neoplasm is the usual cause.

#### THE POSTERIOR FOSSA

A detailed picture of the ventricles and cisterns in the posterior fossa, and the intervening cerebral structures, may be secured by taking roentgenograms when a maximal volume of gas has been introduced into the spaces. This is accomplished during the period of introduction of gas. The following is an account of the procedure:

The patient's head is flexed to thirty or thirty-five degrees, that is, the orbitomeatal line, which serves as a useful index, is inclined downward and forward, making an angle of twenty degrees with the horizontal plane. Filling is commenced in the usual fashion and when approximately 10 c.c. of gas have been injected, a lateral view is taken to show the fourth ventricle and aqueduct, uncomplicated by cisternal shadows. A posteroanterior view is then taken with the central ray directed along the orbitomeatal line (Fig. 8, *a*). Distortion may be avoided if the head is temporarily dorsiflexed so that the orbitomeatal line is horizontal. At this inclination the central ray makes an obtuse angle with the long axis of the fourth ventricle, so the latter is seen on the film as an isosceles triangle (*B*, Fig. 8, *a* and Fig. 9, *a*). The aqueduct extends upward to the third

ventricle. In this posture the anterior and inferior portion of the third ventricle does not fill because the interventricular foramen is relatively high (especially if the head is erect), hence the shadow of the third ventricle is small (Fig. 9, a).

Filling is then continued with the head in the original posture. When the ventricles are replete, gas begins to flow along the medullary and pontine

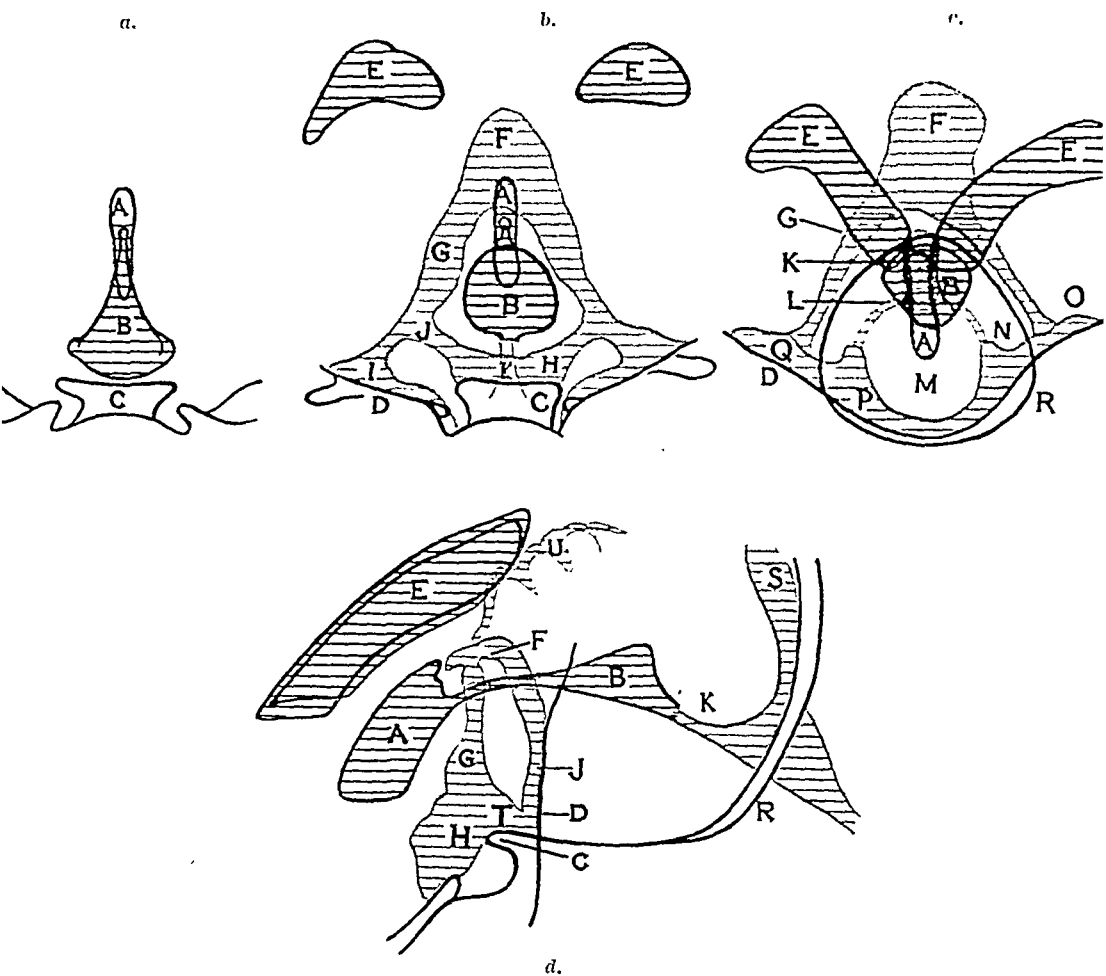


Fig. 8.—The posterior fossa. (a) Posteroanterior view, head flexed fifteen degrees; (b) head flexed thirty-five degrees; (c) head flexed sixty-five degrees; (d) lateral view, head flexed sixty-five degrees; the central ray horizontal in each. A, third ventricle; B, fourth ventricle; C, dorsum sellae; D, petrous temporal bone; E, lateral ventricle; F, cisterna venae magnae cerebri; G, ambient cistern; H, interpeduncular cistern; I, upper part of lateral recess; J, anterior part of ambient cistern; K, anterior part of cisterna magna; L, gas between medulla and cerebellar tonsil; M, medulla; N, flocculus of cerebellum; O, cerebellum; P, medullary cistern; Q, lateral recess; R, foramen magnum; S, dorsal part of cisterna magna; T, pontine cistern; U, gas above cerebellum.

cisterns, and thence into their lateral recesses, and into the interpeduncular and ambient cisterns. A posteroanterior roentgenogram is taken when some 30 c.c. have been injected (Fig. 8, b). The central ray is horizontal, making an angle of thirty-five degrees with the long axis of the skull, and passing through the occipital bone below the external occipital protuberance (Fig. 9, b). The

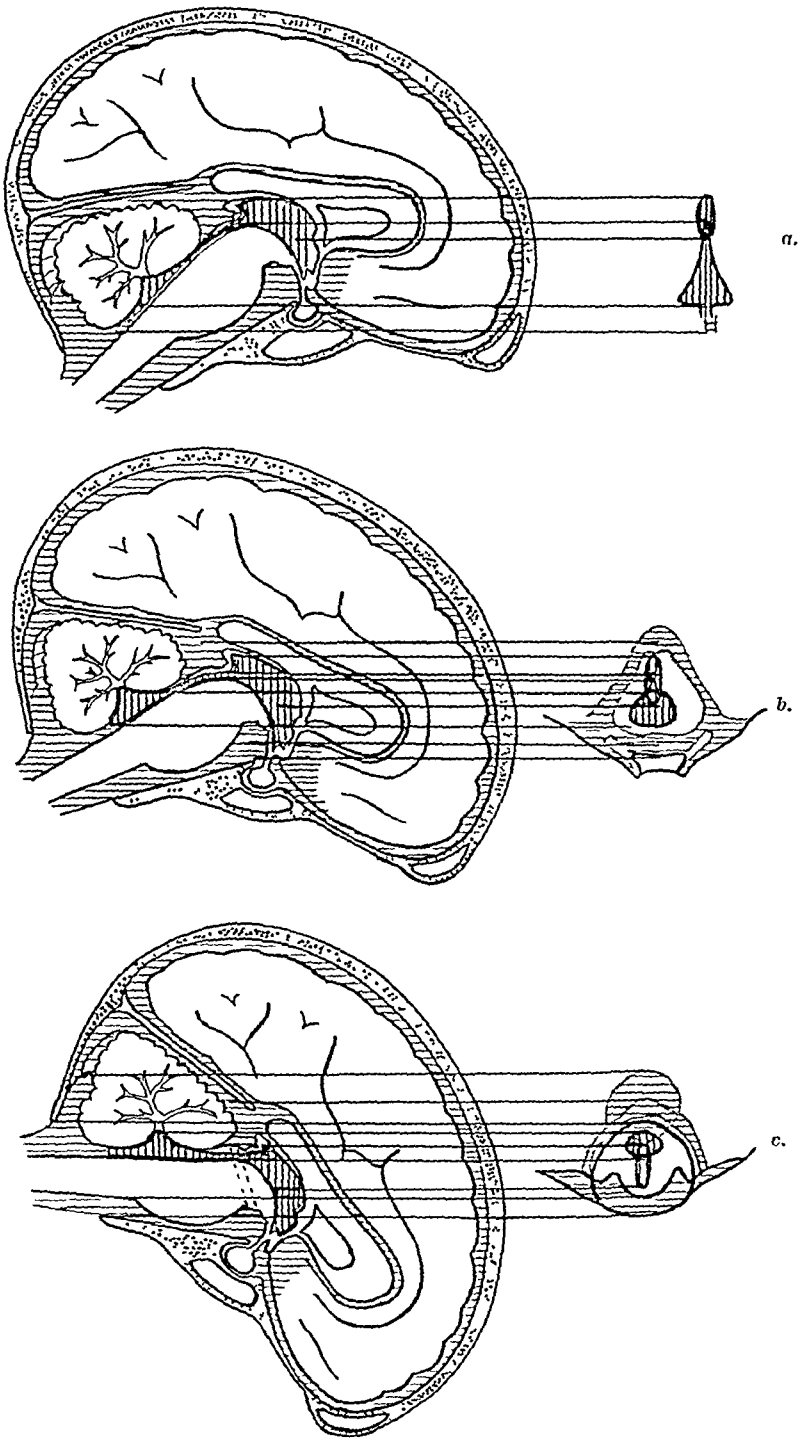


Fig. 9.—Diagrammatic correlation of origin and shadow, the head being flexed to fifteen degrees in *a*, thirty-five degrees in *b*, and sixty-five degrees in *c*.

appearances of the ventricles and of the cisterns have been described separately and are illustrated in Figs. 3 and 5. When both ventricles and cisterns contain gas, the ventricular shadows are thrown into the area representing the mid-brain and cerebral peduncles, encircled by the interpeduncular and ambient cisterns (Figs. 8, *b*, and 9, *b*).

The head is now flexed to sixty-five degrees (so that the orbitomeatal line makes an angle of fifty degrees with the horizontal). An additional 20 c.c. are more rapidly injected, and a posteroanterior view is taken with the central ray horizontal and directed at the foramen magnum. Fig. 10 is a reproduction of a roentgenogram taken in this posture, Fig. 8, *c* is a tracing, and Fig. 9, *c* analyzes the composition of the shadow. The rays are now directed along the



Fig. 10—Posteroanterior view, the head being flexed to sixty-five degrees and the central ray horizontal.

axis of the medulla and pons and more or less parallel with the plane of the basiocciput and basisphenoid (Fig. 9, *c*). Thus, projected into the circle of the foramen magnum, can be seen the cross section of the medulla (*M*, Fig. 8, *c*) and the inferior cerebellar peduncles, outlined by gas in the medullary cistern (*P*), the lateral recesses (*Q*), and the fourth ventricle (*B*). The flocculi of the cerebellum (*N*) are always clearly outlined. Sometimes gas is seen between the medulla and tonsils of the cerebellum on each side (*L*). The dorsal part of the cisterna magna is at a higher level than the other spaces, so its shadow appears at a high level (*F*, Fig. 8, *c*). The ventral part of the cistern is often seen as a dense shadow running downward to the lowest part of the shadow of the fourth ventricle (*K*, Fig. 8, *c*). The long axis of the third ventricle is approximately at right angles to the central ray, and the degree of flexion brings a considerable part of the third ventricle to a lower level than the fourth. Hence the shadow (*A*) is a long one, and extends downward below the fourth ventricle into the



area representing the medulla. The lateral ventricles (*E*) are projected lower than in the previous views. The ventral surface of the pons may sometimes be visible although more usually it is obscured by bone. The lateral recesses (*Q*) are clearly shown. Passing dorsally from the lateral recesses, and more or less parallel with the margin of the foramen magnum, two columns of gas (*G*) can be seen. They converge dorsally in the cisterna venae magnae cerebri (*F*). This appearance is due to gas flowing from the lateral recesses, under the tentorium and ventral to the lobulus quadrangularis of the cerebellum to join the lower part of the ambient cistern. Except in its ventral part this shadow is superimposed upon that of the upper part of the ambient cistern. The two tributaries can be seen in lateral views (*J* and *G*, Fig. 8, *d*) and in the roentgenogram taken with thirty-five degrees of flexion (Fig. 8, *b*). That from the lateral recess runs between *J* and *I* (Fig. 8, *b*) and the ventral part of the ambient cistern between *J* and the interpeduncular cistern (*II*).

Finally, a lateral view is taken in this posture to show the cisterns as well in the ventricles (Fig. 8, *d*). The anteroposterior diameter of the medulla and pons can be measured. The quadrigeminal plate is clearly defined between the aqueduct and the cisterna venae magnae cerebri. The lateral recesses are, in large part, concealed by the density of the petrous temporal bones. The upper parts, underlying the tentorium close to its attachment to the temporal crest can, however, be seen (*J*). The columns of gas converging upon the cisterna venae magnae cerebri may be clearly seen. One (*G*) extends dorsally from the interpeduncular cistern, and the other extends from the upper part of the lateral recess (*J*). Sometimes these two columns fuse, the whole ambient cistern then being filled. The upper surface of the cerebellum may be outlined by gas (*U*) extending dorsally from the cisterna venae magnae cerebri. When the cerebellum is atrophic the whole of the cerebellar subarachnoid space may be filled with gas by continuing the injection with the head well flexed.

## Original Communications

### A STUDY OF THE AZOTEMIA OBSERVED AFTER SEVERE BURNS

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**D**ETERMINATIONS of the plasma nonprotein nitrogen concentration following severe thermal burns have shown marked azotemia which has paralleled the development of the clinical signs of burn toxemia. As these changes were not closely correlated with the oliguria which was sometimes observed, it seemed of interest to investigate the known components of the plasma nonprotein nitrogen separately to see if an explanation for the lack of correlation could be found.

In a series of about 100 patients studied in the various Philadelphia hospitals in 1943 and 1944, the plasma nonprotein nitrogen rose to above 100 mg. per cent in eight patients. All of these patients died, and seven of the eight died with symptoms of toxemia after the second but before the eighth day following the burn. Most of the other patients who died either showed pathologic lesions unrelated to the burn which explained the death, or had nonprotein nitrogen levels of over 80 mg. per cent.

A number of workers have reported a rise in the nonprotein nitrogen of the blood following severe burns,<sup>1-9</sup> but the close association of this rise with the clinical syndrome of burn toxemia has not been adequately stressed. Burn toxemia was distinguished from burn shock by Wilson, MacGregor, and Stewart.<sup>10</sup> The distinction seems valid clinically, but definition of burn toxemia has always been difficult since no quantitative laboratory criteria have been available for its measurement. The association observed in this study between changes in nonprotein nitrogen fractions of the plasma and the clinical symptoms suggests the use of the change in blood chemistry as a laboratory criterion of burn toxemia and as an index of its severity.

#### CLINICAL MATERIAL AND LABORATORY METHODS

From a series of over 100 patients with thermal burns requiring hospitalization, which were studied under a contract between the Office of Scientific Research and Development and the Pennsylvania Hospital, sixteen were selected for detailed analyses of the nonprotein nitrogen content of plasma and urine. Urea nitrogen, uric acid nitrogen, creatinine nitrogen, and alpha-amino acid nitrogen; as well as the total nonprotein nitrogen, were determined separately. The difference between the total nonprotein nitrogen and the sum of the other

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components was called undetermined nitrogen and proved to be of special interest.

The local treatment consisted of the application of bland ointment and pressure dressings. Several of the patients received large volumes of one-sixth molar sodium lactate orally as suggested by Fox.<sup>11</sup> In addition, these patients also received parenteral plasma in amounts adequate to prevent excessive hemoconcentration. We did not feel justified in abandoning the use of plasma in the treatment of shock. Three normal control patients were given 5 L. per day of one-sixth molar sodium lactate for three days, after an initial twenty-four hour control period. Nonprotein nitrogen fractions were studied as in the burned patients (Cases 17, 24, and 30).

Case histories, detailed tabulations of blood and urine analyses from two representative cases, and graphic representations of the plasma nonprotein nitrogen partition for each case follow.

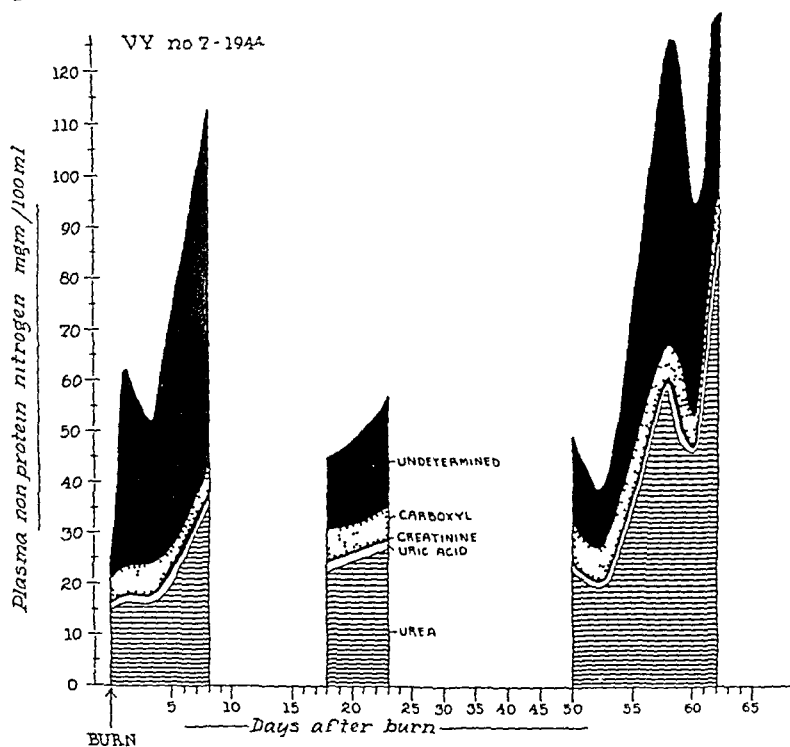


Fig. 1.

#### CASE REPORTS

CASE 7 (V. Y., Fig. 1).—A 43 year old Armenian housewife was admitted at noon on Jan. 6, 1944, twenty minutes after she had sustained a 55 per cent third degree burn of the body and extremities while cleaning a dress with gasoline. She was given morphine, and intravenous plasma was started while she was in the operating room. The burned areas were superficially débrided and petrolatum gauze and pressure dressings applied. Hematocrit was 37 per cent on admission and rose to 56 per cent eight hours after the accident. This was the highest value attained. The patient was given 2.5 L. of plasma and 300 c.c. of saline solution intravenously. In the first eighteen hours she received 3 L. of one sixth molar sodium lactate orally. She developed thrombosis of the right deep femoral vein with marked spasm of the artery, but circulatory embarrassment was somewhat relieved by use of an oscillating bed.

The patient remained febrile and disoriented for three days. On the third day she had two periods of apnea, lasting ten and three minutes, respectively, during which artificial respiration was required. She then became rational on the fourth day, and her general condition improved. On the thirty-fourth day the patient had a series of severe hemorrhages that arose from an apparently spontaneous rectovaginal fistula and rectal ulceration. This was controlled by packing and transfusion.

In spite of a high protein diet, tube feedings, and repeated infusion of plasma and blood, the patient lost about thirty pounds of weight. On the fifty-ninth day the patient became semistuporous and died on the sixty-second day, of multiple pulmonary emboli.

Post-mortem examination revealed moderate fatty infiltration of the liver and evidence of toxic nephrosis that occurred during the toxemia. Tubular damage was still evident, but regenerative processes were marked. Adrenals showed necrosis of the inner zone of the cortex.

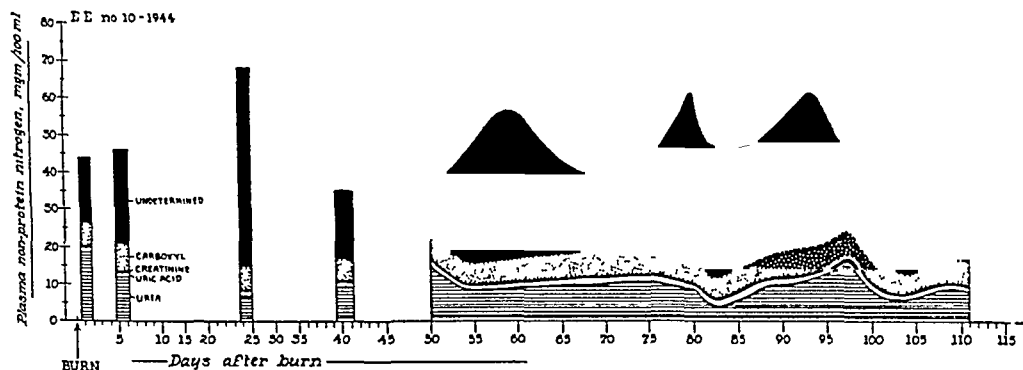


Fig. 2.

CASE 10 (E. E., Fig. 2).—A 6-year-old white boy sustained a 30 per cent third degree flame burn of the legs. Burned areas were treated by superficial débridement and petrolatum gauze and pressure dressings. Intravenous plasma was given. The patient sustained only moderately severe shock but thereafter became markedly toxic. Temperature rose steadily to 104° F. on the fifth day and the pulse was 160. Sulfadiazine was started on the fourth day and thereafter the temperature fluctuated between 101 and 99° F. The patient took over 1,500 c.c. of one-sixth molar sodium lactate orally during the first seven days. The patient's nutrition remained poor in spite of all efforts until the areas healed. Skin grafts were applied on the forty-seventh, fifty-sixth, and sixty-fourth days.

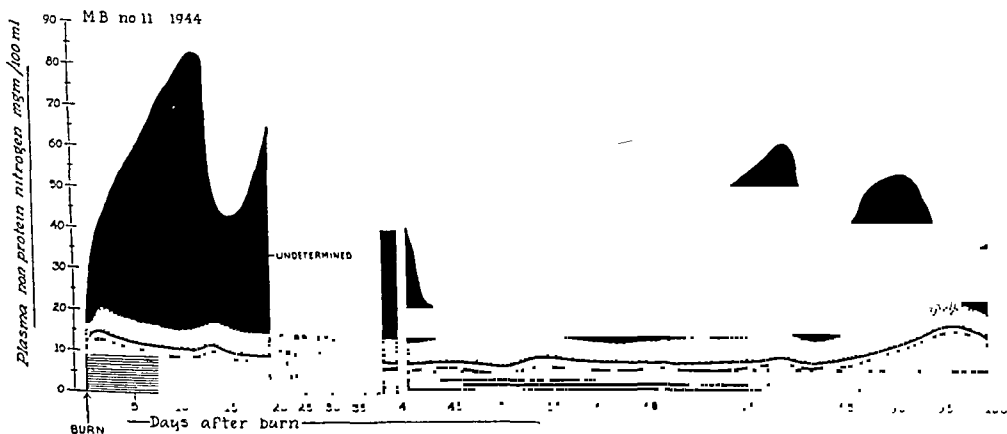


Fig. 3.

CASE 11 (M. B., Fig. 3).—A 50-year-old white woman sustained a 25 per cent scald of the legs and right arm. The hematocrit was 42 per cent twelve hours after the burn. The patient was given plasma intravenously (1,500 c.c. the first day and 750 c.c. the second day) and also received 3 to 5 L. of sixth molar sodium lactate orally daily for the first seven days. Temperature rose to 101° F. but the patient was not remarkably toxic. The temperature became normal on the third day and the patient improved rapidly. Skin grafts were applied on the thirty-third and fifty-first days.

CASE 12 (D. G., Fig. 4).—A 27-year-old colored man sustained a 30 per cent flame burn of the head, shoulders, and arms. Petrolatum gauze and pressure dressings were applied, and the patient was given intravenous plasma. Eighteen hours after the burn the patient began to have marked respiratory distress, and thirty-six hours after the accident tracheotomy was necessary. The patient improved thereafter, although he was markedly toxic for five days. He was given from 1 to 5 L. of one-sixth molar sodium lactate orally during the first ten days. The tracheotomy tube was removed thirty-six days later and skin grafts applied on the fifty-third day. See Tables I and II.

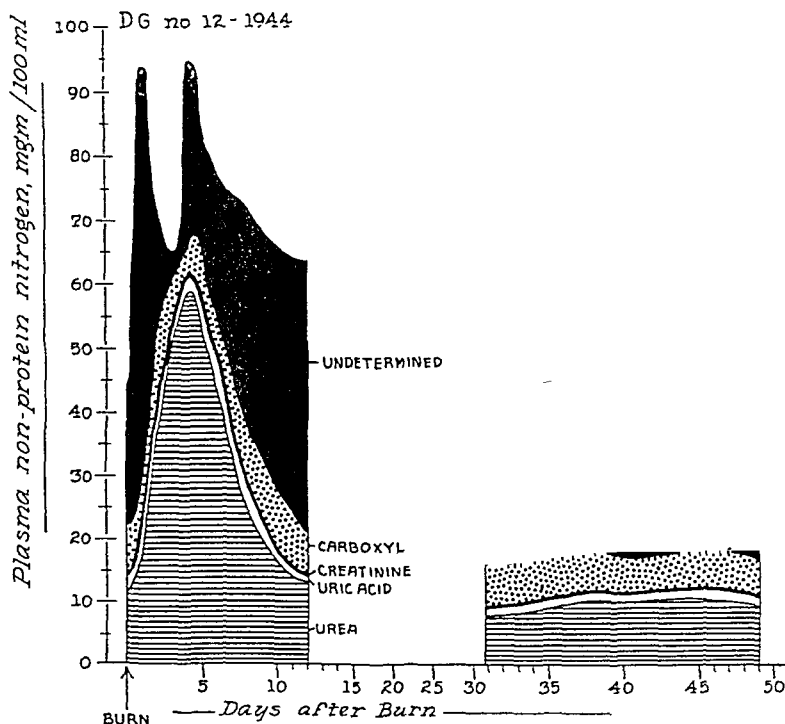


Fig. 4.

CASE 14 (N. A., Fig. 5).—A 4½-year-old Italian child received a 12 per cent scald of the left arm and side. She was not brought to the hospital until twenty-five hours after injury, at which time the burns were dressed with petrolatum gauze and pressure dressings. The child was given 100 c.c. of plasma the day of admission and 250 c.c. the following day. She showed only moderately severe toxemia.

CASE 17 (J. W., Fig. 6).—A 27-year-old white man was a control patient. Blood specimens and urine collections were taken for twenty-four hours, after which the subject drank 5 L. of one-sixth molar sodium lactate orally daily for three days. A positive Chvostek sign was noted forty-eight to seventy-two hours after the administration of sodium lactate.

CASE 19 (C. C., Fig. 7).—A 44-year-old white man received a 45 per cent scald and flame burn of the trunk, head, and extremities. The burned areas were sprayed with triple dye. Intravenous plasma was administered. This patient suffered deep shock, and after

TABLE I. PLASMA ANALYSES (CASE 12)

TIME AFTER BURN	HEMATOCRIT (PER CENT)	VAN DEN BERGH	PROTEIN (GM. PER 100 C.C.)	ALBUMIN-GLOBULIN RATIO	NONPROTEIN NITROGEN (MG. PER 100 C.C.)	UREA NITROGEN (MG. PER 100 C.C.)	URIC ACID NITROGEN (MG. PER 100 C.C.)	CREATININE NITROGEN (MG. PER 100 C.C.)	CARBOXYL NITROGEN (MG. PER 100 C.C.)	INDETERMINED NITROGEN (MG. PER 100 C.C.)	CHLORIDES (MG. PER 100 C.C.)	CARBON-DIOXIDE COMBINING POWER (VOL. PER CENT)
1 hr.		1.0	7.21		44.3	16.0	2.6	0.7	7.5	17.50		33
6 hr.	52	6.36		93.5	12.0		0.7	7.0	71.2			33
18 hr.	69					22.0	2.6	6.9				
19 hr.	69	0.9	8.00		22.0						98.0	
20 hr.	56		6.8		41.0		2.8	0.9				
21 hr.	60	0.4	6.7		28.0		1.2	0.9	6.5	47.4		37
2 days	56	1.2	8.10		38.0		1.7	0.9	7.0	25.7		
3 days	50	0.4	7.01	1.0	51.0		1.3	0.9	7.5	3.7		
4 days	48	0.5	6.63		59.0		2.3	0.9	7.5	21.6	95.6	37
5 days	48	0.7	6.80		80.0		0.7	0.9	6.5	17.6	96.2	
18 days	42	0.5	5.45	0.6	65.3	13.0				42.6	103.0	
20 days	41	0.1	7.01	1.0		11.0						
24 days		0.1	5.38	0.9		13.0						
27 days		0.1	6.1	1.2		9.0	0.9	0.4			102.0	
29 days						8.0		0.4				
31 days		0.1	7.04	1.2	43.0	8.0	0.9	0.4		37.2	100.2	
38 days	43		7.07	1.4	46.0	10.0		0.5		28.2	96.0	
46 days	53				39.3	10.0	1.5	0.3		20.5		
49 days	46				31.3	9.0	1.6	0.4		13.8	89.8	

TABLE II. URINE ANALYSES (CASE 12)

DAY AFTER BURN	12 HR. VOLUME	SPECIFIC GRAVITY	ALBUMIN (GM. PER 12 HR.)	NONPROTEIN NITROGEN (GM. PER 12 HR.)	UREA NITROGEN (GM. PER 12 HR.)	UREA CLEARANCE (PER CENT OF AVERAGE NORMAL FUNCTION)	CITRIC ACID NITROGEN (GM. PER 12 HR.)	CREATININE NITROGEN (GM. PER 12 HR.)	CREATININE NITROGEN (GM. PER 12 HR.)	UNDETERMINED NITROGEN (GM. PER 12 HR.)	CHLORIDES (GM. PER 12 HR.)
1	1,740	1.008	0.120	20.000	14.700	45	0.067	0.012	0.086	5.135	1.60
1 1/4	1,230	1.030	0.086	16.100	12.500	47	0.105	0.014	0.114	3.367	1.35
2	2,000	1.025	0.140	28.200	19.900	89	0.085	0.011	0.042	8.162	
2 1/2	790	1.036	0.158	6.808	4.100	38	0.047	0.009	0.025	2.719	0.80
3 1/2	890	1.034	0.260	11.200	8.500	37	0.023	0.007		2.651	1.03
4	580	1.035	0.045	8.100	7.700	37	0.037	0.010		0.340	6.60
4 1/2	550	1.008	0.052	1.750	1.070	8	0.021	0.005	0.007	0.637	0.60
5	380	1.030	0.270	4.700	4.200	28	0.029	0.015		0.440	0.43
6 1/2	760	1.040	0.170	13.500	9.500	44	0.119	0.036	0.025	3.820	1.20
7	380	1.034	0.053	6.600	4.200	28	0.017	0.008	0.025	2.350	0.62
13 1/2	1,070	1.023	0.750	10.400	6.600	103	0.100	0.036		3.644	3.00
16 1/2	620	1.026	0.050	6.350	4.340	100				1.900	3.15
20 1/2	990		0.080	0.720	0.690	120	0.026	0.009	0.014	0.000	
23 1/2	1,015	1.014	0.710	3.540	2.120	53		0.007	0.003	1.354	
27 1/2	95	1.043	0.033	1.160	0.310	26	0.081	0.005	0.001	0.763	
30 1/2	250	1.010		0.710	0.630	32		0.002	0.015	0.000	1.40
34 1/2	345	1.020	0.012	1.950	2.920	100	0.162	0.072	0.015	1.779	
36 1/2	1,080	1.019		6.650	2.350	40		0.011	0.000	4.127	
41 1/2	580	1.019		4.120	3.200	90	0.162	0.023	0.006	0.729	
44 1/2	360	1.020	0.250	4.550	2.000	80		0.016	0.013	2.359	2.40

recovery from this phase was markedly toxic. On the third day he became comatose. Renal shutdown was almost complete and the patient died on the fourth day. Post-mortem examination showed some recent hepatic fatty infiltration superimposed on an old portal cirrhosis. Toxic nephrosis was marked with almost complete tubular destruction. Adrenals showed edema and necrosis of the inner zone of the cortex. The brain showed ganglion cell degeneration and edema.

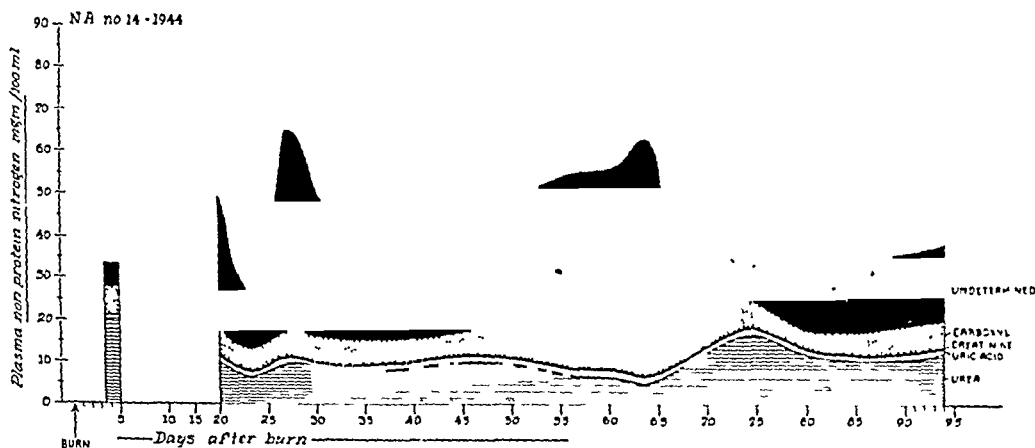


Fig. 5.

### CONTROL CASES

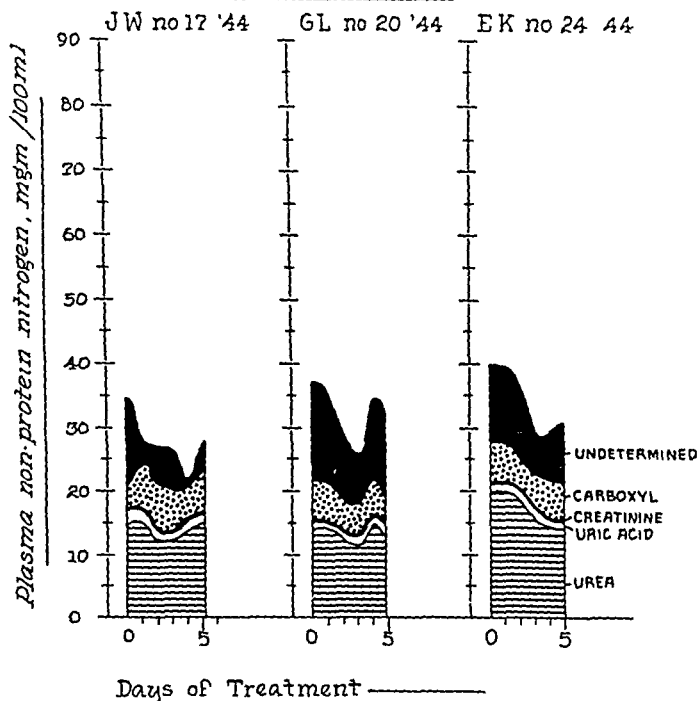


Fig. 6.

CASE 20 (G. L., Fig. 6).—A 24-year-old white man was another control patient and was treated just as was the patient (J. W.) in Case 17.

CASE 24 (E. K., Fig. 6).—A 38-year-old woman was also a control.

CASE 25 (M. B., Fig. 8).—A 50-year-old colored woman received a 20 per cent second and third degree burn of the head, arms, and shoulders. Petrolatum gauze and pressure



dressings were applied. Intravenous plasma (500 c.c.) was given the first day. In addition she received 3 L. of one-sixth molar sodium lactate orally during the first nine days after being burned. The patient became markedly toxic, although shock had not been severe. Urine output was poor during the first two days but then improved. Temperature rose steadily toward 106° F. on the sixth day, but thereafter her condition improved quickly. Skin grafts were applied on the thirteenth, forty-first, and eighty-second days. See Tables III and IV.

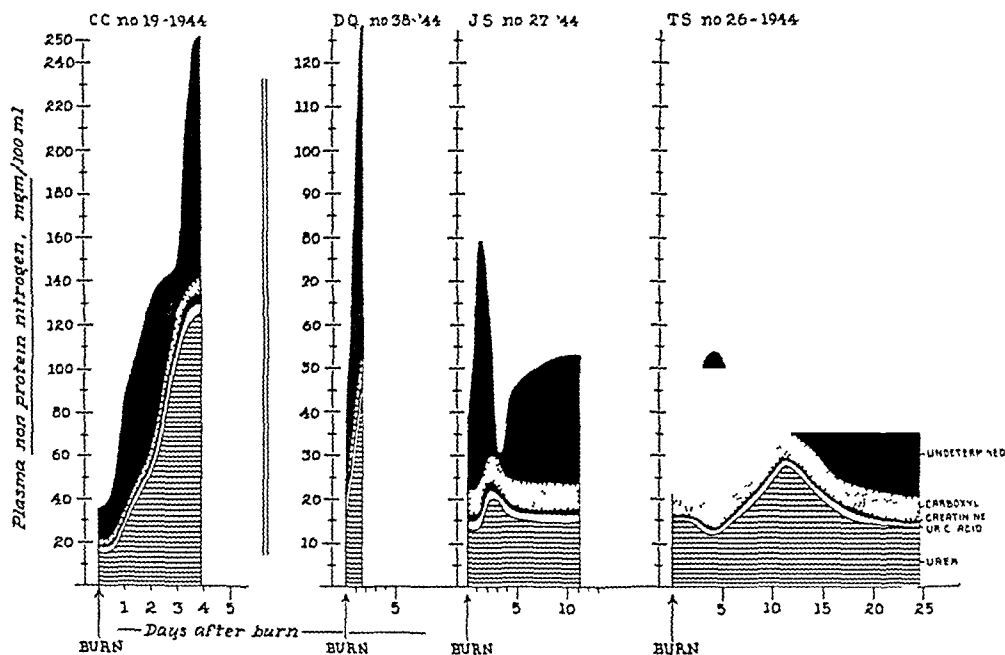


Fig. 7.

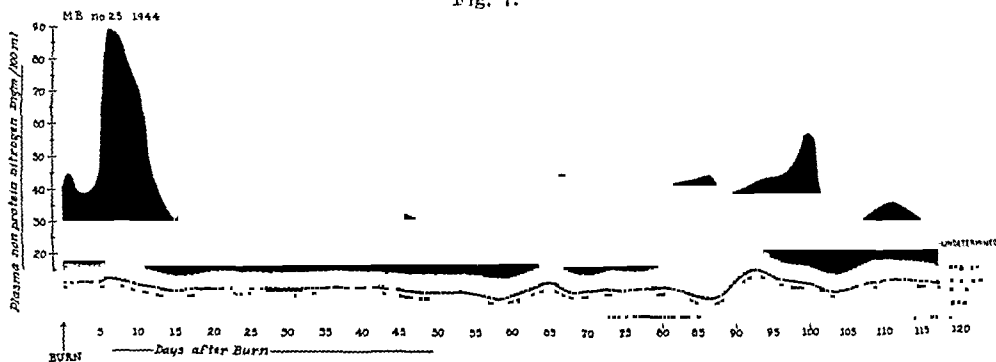


Fig. 8.

CASE 26 (T. S., Fig. 7).—A 22 year old white man sustained an 18 per cent third degree burn of both arms, the face, and chest. The patient received 750 c.c. of plasma the first day, 500 c.c. the second, 500 c.c. the third, and 750 c.c. the fourth day. Burns were tanned with methyl red. The patient was moderately toxic for the first four days. He had bronchopneumonia from the fifth to tenth day but thereafter improved rapidly.

CASE 27 (J. S., Fig. 7).—A 4 year-old white boy received 18 per cent second and third degree burns of the arms, face, and trunk. The burns were dressed with petrolatum gauze and pressure dressings. Intravenous plasma was administered. Hematocrit eighteen hours after the burn was 55 per cent. The boy was quite toxic and the urinary output poor for the first five days. Thereafter he made an uneventful recovery. Skin grafts were not necessary.

TIME AFTER BURN	HEMATOCRIT (PER CENT)	VAN DEN BERGH	PROTEIN (G/L, PER 100 G.C.)	ALBUMIN-GLOBULIN RATIO	NONPROTEIN NITROGEN (MG. PER 100 G.C.)	UREA NITROGEN (MG. PER 100 G.C.)	TRIC ACID NITROGEN (MG. PER 100 G.C.)	CREATININE NITROGEN (MG. PER 100 G.C.)	CARBONYL NITROGEN (MG. PER 100 G.C.)	UNDETERMINED NITROGEN (MG. PER 100 G.C.)	GILLOIDES (MG. PER 100 G.C.)	CARBON-DIOXIDE CONTAINING POWDER (VOL. PER CENT)
12 hr.	40	0.1	5.54		38.3	10.0			6.0	29.3	87.0	39
1 day	143	0.1	7.07		45.3	10.0			5.8	27.5		
2 days	48	0.3	6.46		38.8			0.5	5.3	27.1		
4 days	45		6.76	1.0	39.1					27.6		
55 days	45	0.1	6.12		44.6					27.1		
66 days			5.07		80.0	11.0		0.6	3.5	70.4		
9 days	42				40.0	11.0				21.5		
11 days	35		5.5			9.0		0.4		17.1		
15 days	39				31.6	7.0				24.1		
17 days	39		7.14		39.6	8.0				22.8		
19 days	49		7.10		17.0	8.0			3.5	26.1		
23 days	39		8.3	0.7	48.3	7.0				39.0		
36 days	33				40.6	7.0				18.0		
37 days	33	0.1	5.07	0.7		9.0	0.7			85.0		
39 days	38	0.1	5.04	0.8	53.0					93.6		
43 days		0.1	5.38	0.9		8.0		0.3		96.0		
46 days			4.41	1.1	31.0	7.0				26.8		
50 days		0.1			33.0	5.0			6.0	96.2		
54 days	37	0.2			34.0	10.0				103.0		
58 days	32	0.2			44.0	7.0				94.3		
65 days	40	0.1			44.3	8.0				27.3		
68 days	43	0.1	3.01	1.1	39.6	8.0				27.6		
72 days	42	0.1			36.3	8.0				33.3		
74 days	44	0.1	6.94		42.3	8.0				21.8		
79 days	40	0.2			42.6	5.0				21.1		
82 days	41	0.2			45.6	7.0	1.1	0.4	6.0	26.8		
86 days	49	0.1			39.3	14.0				41.2		
88 days	39	0.1			42.6	11.0				20.2		
92 days	44	0.1			38.6	10.0	0.8	1.0		13.9		
99 days	41	0.2	7.19	1.1	34.6	9.0		0.6		17.6		
103 days					29.6	11.0				13.5		
106 days	41	0.1			30.3	9.0				98.7		
110 days					36.0	11.0				101.5		
117 days	38	0.1	7.10		29.6	9.0		0.3				

TABLE IV. URINE ANALYSES (CASE 25)

DAY AFTER BURN	12 HR. VOLUME	SPECIFIC GRAVITY	ALBUMIN (GM. PER 12 HR.)	NONPROTEIN NITROGEN (GM. PER 12 HR.)	UREA NITROGEN (GM. PER 12 HR.)	UREA CLEARANCE (PER CENT OF AVERAGE NORMAL FUNCTION)	TRIC ACID NITROGEN (GM. PER 12 HR.)	CREATININE NITROGEN (GM. PER 12 HR.)	UNDETERMINED NITROGEN (GM. PER 12 HR.)	CHLORIDES (GM. PER 12 HR.)
2	840	1.022	0.155	7.600	3.240	75	0.101	0.007	0.032	0.93
2½	1,300	1.017	0.870	5.270	3.260	50			1.716	2.06
3	1,930	1.015	1.120	5.150	2.700	50	0.249	0.131	2.062	2.30
3½	850	1.020	0.610	2.300	1.430	33		0.020	0.033	1.26
4	980	1.034	0.316	4.700	2.700	59	0.138	0.188	1.028	
7½	1,222	1.018	0.800	5.100	2.740	55			1.950	1.46
8	1,660	1.019	0.600	4.550	1.970	37	0.176		2.187	1.66
8½	2,860	1.026	0.740	5.100	1.440	27		0.117	0.154	
9	1,260	1.036	0.450	4.800	2.120	40	0.097	0.011	2.367	1.46
9½	1,040			2.710	1.160	25			1.020	1.52
10	890	1.025	0.580	1.950	1.250	28	0.012		0.533	1.37
10½	1,800	1.016	0.130	3.460	3.250	75			0.000	
11	540			1.680	0.760	23	0.047	0.007	0.919	0.52
12½	440	1.008	0.158	0.790	0.740	25	0.026	0.003	0.019	
14½	1,145			2.890	1.830	38	0.058	0.026	0.865	1.20
39	110	1.020		0.700	0.460	30	0.004		0.216	
39½	260			0.720	0.510	25		0.019	0.160	
40	110			0.640	0.540	45		0.003	0.033	
49	600	1.014	0.240	2.350	2.100	70	0.064	0.006	0.171	
55	320	1.020	0.112	1.400	1.300	100		0.001	0.008	1.60
61½	710			1.600	1.540	44			0.000	
62	1,650	1.016	0.230	3.800		40	0.077	0.014	2.159	
65	360	1.010		2.150	1.610	45	0.007	0.006	0.473	1.87
68	520	1.011	0.150	1.370	1.090	47		0.005	0.259	2.00
72	200	1.014	0.140	1.290	1.200	75	0.026	0.003	0.000	
82	170	1.024	0.038	1.300	0.910	50	0.098	0.005	0.007	
100	210	1.012	0.151	0.690	0.610	35		0.001	0.004	
101	240	1.014		0.920	0.510	55		0.001	0.000	0.55
107	990	1.009	0.040	2.860	2.370	55	0.197	0.014	0.038	

CASE 32 (E. W., Fig. 9).—A 25-year-old white woman received a 12 per cent scald of the right arm and shoulder. Petrolatum gauze and pressure dressings were applied. The patient was given 750 c.c. of plasma the first day. An oral intake of over 2 L. of one-sixth molar sodium lactate was maintained daily for the first seven days. Toxemia was only mild clinically. No skin grafts were necessary.

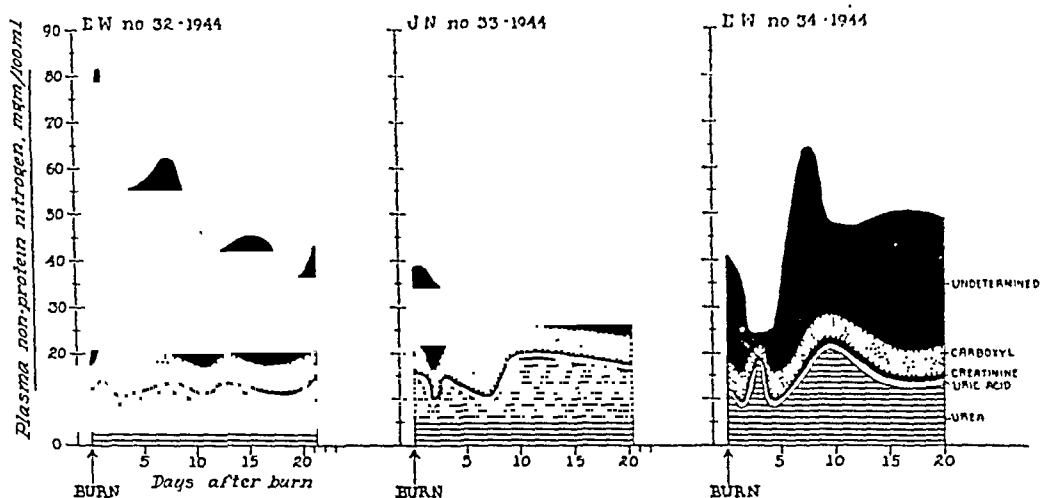


Fig. 9.

CASE 33 (J. N., Fig. 9).—A 58-year-old white man received a 20 per cent second and third degree burn of arms, shoulders, and face. Burns were dressed with boric acid ointment and pressure dressings, and he was given 750 c.c. of plasma the first day. The patient showed moderate toxemia for five days and then improved. No skin grafts were necessary but healing was slow.

CASE 34 (E. W., Fig. 9).—A 42-year-old white man received a 20 per cent second and third degree burn of the head, shoulders, and arms. Burns were dressed with boric acid ointment and pressure dressings. He was given intravenous plasma. He showed fairly severe toxemia for five days with oliguria and some fever but eventually recovered completely without the necessity for skin grafts.

CASE 38 (D. Q., Fig. 7).—A 43-year-old white man received a 40 per cent third degree burn of the head, arms, and legs. Burns were dressed with boric acid ointment and pressure dressings, and intravenous plasma was administered. Urine output remained poor and the patient showed severe toxemia with disorientation. On the third day he seemed to be improving, when he suddenly died in respiratory failure.

Post-mortem examination revealed very little liver damage but a moderately severe toxic nephrosis and necrosis of the inner zone of the adrenal cortex. The brain showed marked edema with ganglion cell degeneration.

CASE 42 (W. B., Fig. 10).—A 65-year-old man received a 10 per cent second and third degree burn of the face and right hand. The areas were dressed with boric acid ointment. No plasma was necessary. The patient felt slightly nauseated for five days, although he showed no shock. Wounds were dressed with gauze.

CASE 43 (H. T., Fig. 10).—A 40-year-old white man received a 12 per cent second and third degree scald of the right arm and shoulder. He was very drowsy and nauseated for five days, although he showed no shock. Wounds were dressed with petrolatum gauze. No plasma was necessary.

CASE 44 (A. S., Fig. 10).—A 72-year-old woman sustained a 35 per cent flame burn of the head, arms, and shoulders. Burned areas were dressed with petrolatum gauze and

pressure dressings and intravenous plasma was administered. The patient was given 5 L. of one-sixth molar sodium lactate solution orally between the first and second days. Urinary output remained good. The patient became disoriented on the second day and showed marked toxemia. She improved somewhat on the fourth day but died of respiratory failure on the fifth day.

Post-mortem examination showed fatty infiltration of the liver, moderately severe toxic nephrosis, and marked cerebral edema and ganglion cell degeneration in the cortex and hypothalamus.

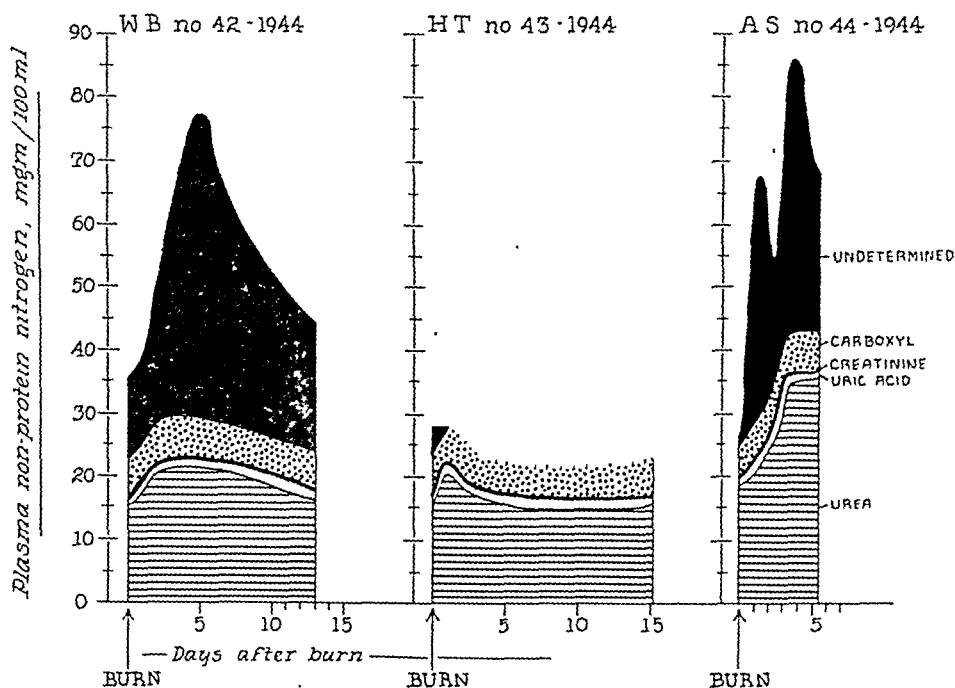


Fig. 10.

Blood specimens were collected in Sanford-Magath hematocrit tubes with small amounts of heparin or sodium oxalate powder. The tubes were centrifuged within one hour of taking the blood and the supernatant plasma was drawn off.

Twelve-hour urine specimens were collected under toluene and kept at a low temperature until examined. Specimens from women patients were collected by means of indwelling catheters.

Serum bilirubin levels were determined by the indirect van den Bergh reaction<sup>12, 13</sup> using potassium permanganate solutions as the colorimetric standard. These determinations were run within ten hours of the time the blood was taken, and in all cases serum or plasma was removed from contact with the cells within one hour.

Plasma protein concentrations were determined by the falling drop method of Barbour and Hamilton.<sup>14</sup> Some protein concentrations and the albumin-globulin ratios were determined by the biuret method.<sup>15, 16</sup> Urinary albumin levels were determined by precipitation with Tosehyia's reagent.<sup>17</sup>

Nonprotein nitrogen levels of plasma and urine were determined by acid digestion and direct nesslerization according to the method described by Folin and Denis<sup>18</sup> and Wong.<sup>19</sup>

Blood urea nitrogen was converted to ammonia by urease and then determined colorimetrically according to the method of Folin and Wu.<sup>20</sup> The urine urea nitrogen was also converted to ammonia by urease, and then the total ammonia content titrated, thus giving urea plus ammonia nitrogen together.

Uric acid levels of blood and urine were determined colorimetrically after treatment with cyanide.<sup>21</sup>

Plasma creatinine and urine creatinine levels were determined by the method of Folin.<sup>22</sup> Total creatinine levels of urine were determined by oxidation of aliquots with picric acid. The urine creatine level was obtained by subtraction of the figure obtained in routine creatinine determination from that obtained after picric acid oxidation of the creatine to creatinine.

Alpha-amino nitrogen, representing the nitrogen from the alpha amino acids, was determined on plasma following the method of MacFadyen.<sup>23</sup> These determinations were carried out only on plasma.

The balance of the nonprotein nitrogen fraction remaining after subtraction of the nitrogen in urea, uric acid, creatinine, and alpha-amino acids was labeled "undetermined nitrogen." Because of the constancy of values obtained for uric acid, creatinine, and carboxyl nitrogen, these determinations were not made as frequently as those for urea and total nonprotein nitrogen. Values on intervening days were obtained by interpolation.

Estimation of the area burned in a given patient was based on the method of Berkow.<sup>24</sup>

## RESULTS

All patients studied since January, 1943, who had plasma nonprotein nitrogen levels of over 100 mg. per cent of plasma died. An additional thirteen patients died with somewhat lower levels. Of this group two had been burned on contact with high voltage electric current and were thought to have died of the effects of the passage of the electric current, three died of rapidly developing shock, and three of pre-existing disease. The remaining five patients had plasma nonprotein nitrogen levels of over 80 mg. per 100 c.c. of plasma. In Fig. 11 is shown the correlation between plasma nonprotein nitrogen and mortality. It also shows that no patient in the series having more than one-third of the body surface involved by third degree burns survived.

Fifty to eighty per cent of the increase in the nonprotein nitrogen of plasma was due to the undetermined fraction. The only patients showing a fairly marked rise in urea nitrogen were those in whom marked oliguria was noted clinically. In most cases the rise in blood urea nitrogen, the slight rise in uric acid nitrogen and in creatinine nitrogen in severe burns, and the small alpha-amino nitrogen component were all more or less constant.

The carbon dioxide combining power of the plasma showed a tendency to drop in the early stage of the burn, but usually returned to normal within forty-eight hours. Plasma chlorides were not remarkably reduced as a whole, although in severe burns there was a definite depression (Davidson,<sup>25, 26</sup> Underhill and associates<sup>27-31</sup> and Rosenthal<sup>32</sup>).

Correlation of the output of nonprotein nitrogen in the urine with the severity of the burn was not as close. There was some increase in nonprotein nitrogen excretion on the first few days and again toward the end of the period of toxic symptoms. The excretion of nonprotein nitrogen rose during the phase of clinical toxemia at some point within the first ten days after injury and then dropped between the seventh and twelfth days, usually corresponding with an amelioration in the clinical signs of toxemia. However, a number of patients with severe burns and a good urinary output did not excrete excessively large

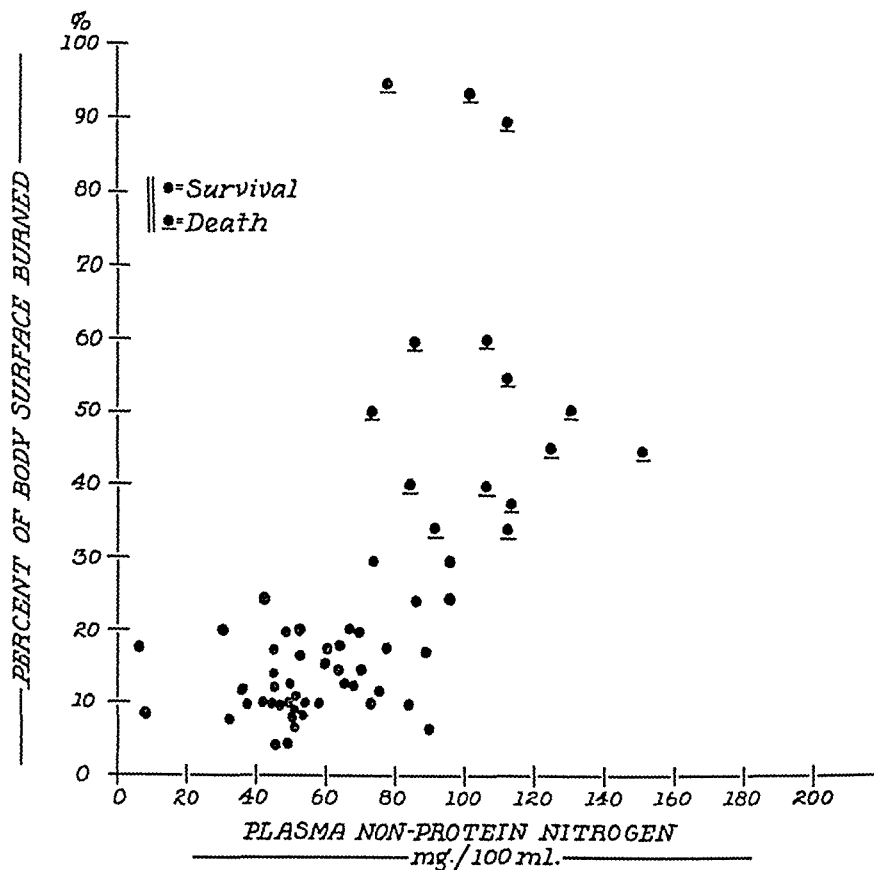


FIG. 11.

amounts of nonprotein nitrogen in the urine. Thirty to fifty per cent of the increase in urinary nonprotein nitrogen was undetermined nitrogen and most of the balance was urea and ammonia nitrogen. There was an increased excretion of creatinine and creatine during the acute phase of toxemia, but this accounted for only a small part of the nitrogen. Uric acid nitrogen excretion remained relatively constant for each patient. Albuminuria was not excessive.

There was a decrease in urea clearance during the stage of toxemia. The tendency toward decreased urea clearance, and also a reversal of the albumin-globulin ratio, persisted in patients having extensive third degree burns until the granulating areas were covered with skin.

Transfusion of whole blood or plasma caused a slight rise in the nonprotein nitrogen fraction. It might be considered possible that the plasma and urinary nonprotein nitrogen elevations observed in toxemia were due to the massive infusion of plasma necessary to combat shock. However, similar changes in the plasma nonprotein nitrogen were observed in patients who received no plasma. One patient (Case 42) with a 10 per cent burn had a plasma nonprotein nitrogen elevation of 42.0 mg. per cent and another (Case 43) with a 12 per cent burn had an elevation of 40.0 mg. per cent above the normal of 35.0 mg. per cent.

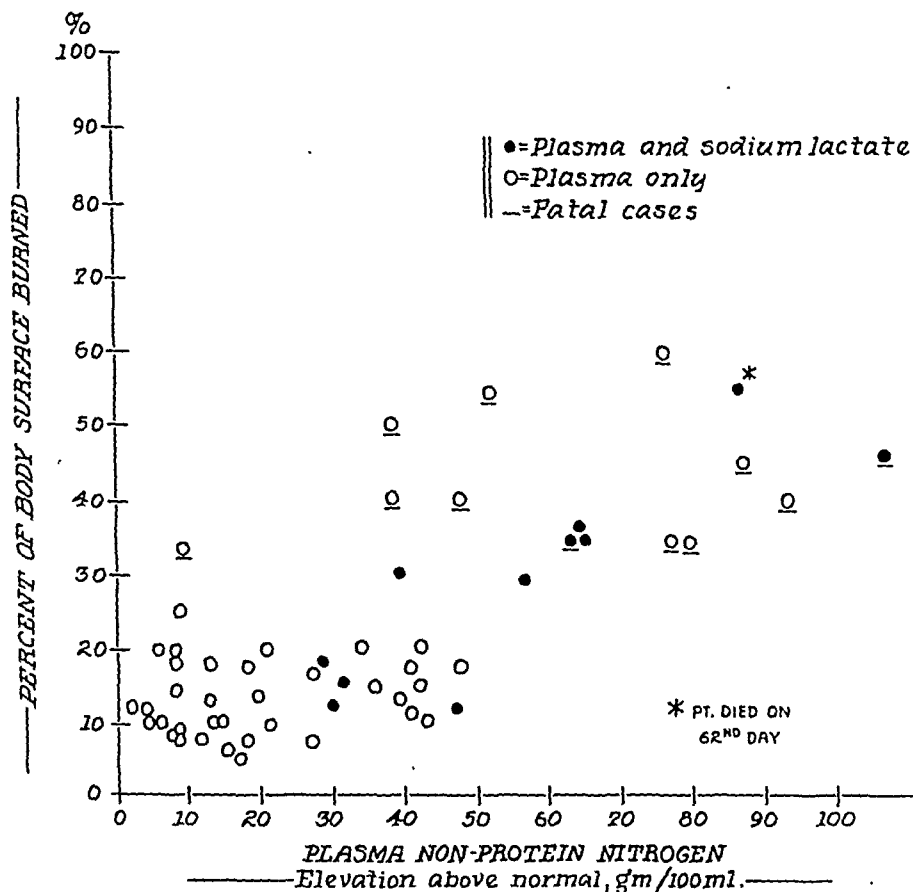


Fig. 12.

It was hoped that the large fluid intake of the patients treated with sodium lactate solution might prevent oliguria and prevent or greatly reduce the rise in the nonprotein nitrogen concentration in the plasma. It did appear to augment the urinary output, but the effect on the nonprotein nitrogen concentration was disappointing. No significant difference could be established in the series of patients treated (Fig. 12).

## DISCUSSION

Wilson, MacGregor, and Stewart<sup>10</sup> stressed the evidence of liver damage, in their paper in 1938, and changes in liver function were reported by Wolff,



Elkinton, and Rhoads<sup>33</sup> in 1940. However, Wells<sup>14</sup> and Wells, Humphrey, and Cole<sup>55</sup> showed that tannic acid could produce such damage and the subsequent papers of Hartman and Romence<sup>16</sup> and Erb, Morgan, and Farmer<sup>37</sup> leave little

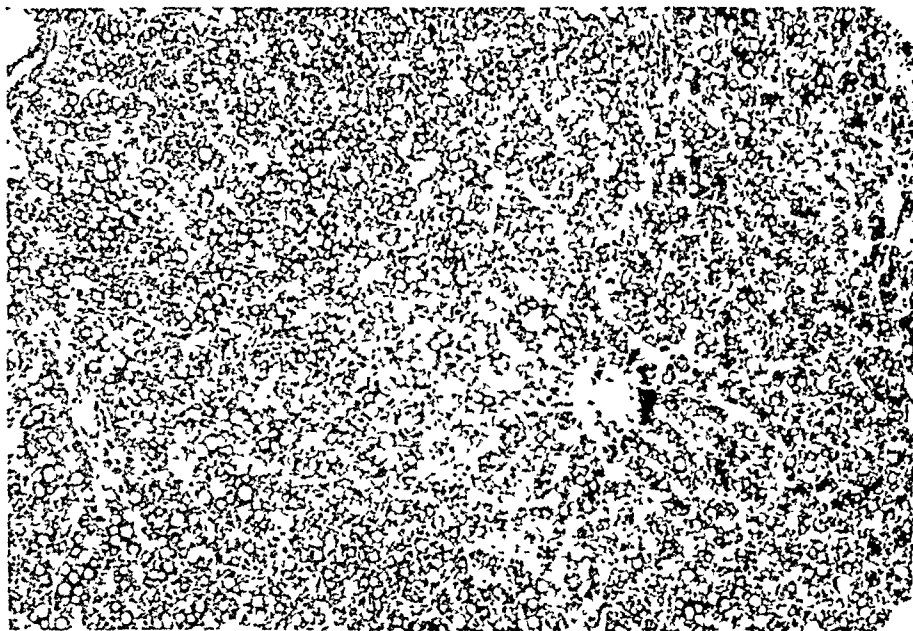


Fig. 13 (L. C., Case 23).—Liver; marked fatty degeneration ( $\times 180$ ).



Fig. 14A (C. C., Case 19)—Kidney, selective destruction of tubular epithelium ( $\times 180$ ).

doubt that most of the severe liver necrosis seen after burns was due to the use of tannic acid in the local treatment. Furthermore, Hartman and Romence

present data indicating that some of the other tanning agents may have had a similar influence.

Since the abandonment of tanning agents in the local treatment, much less disturbance of liver function has been found.<sup>28</sup> There is, however, some dis-

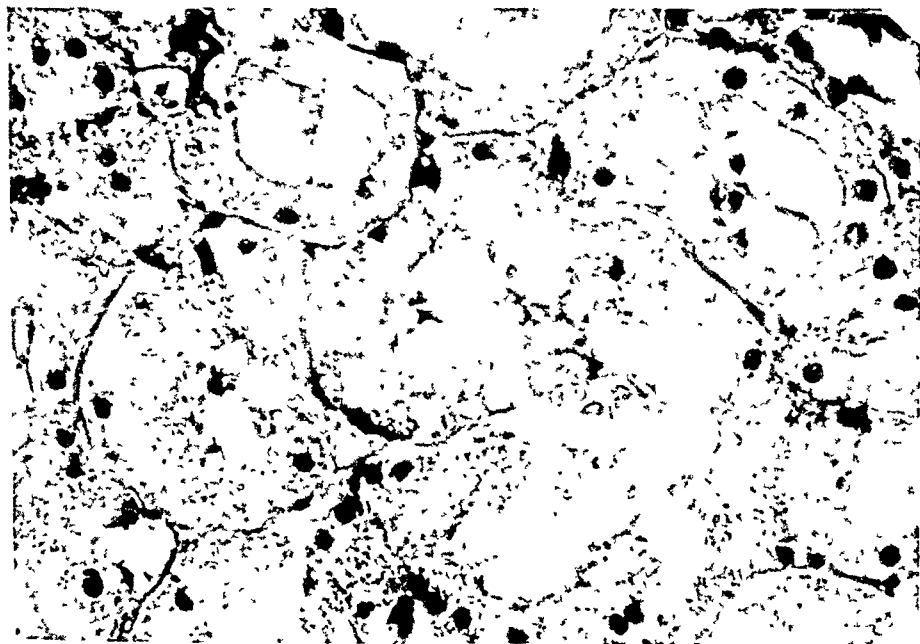


Fig. 14B (C. C., Case 19).—Kidney; vacuolization and autolysis of tubular cells ( $\times 700$ ).

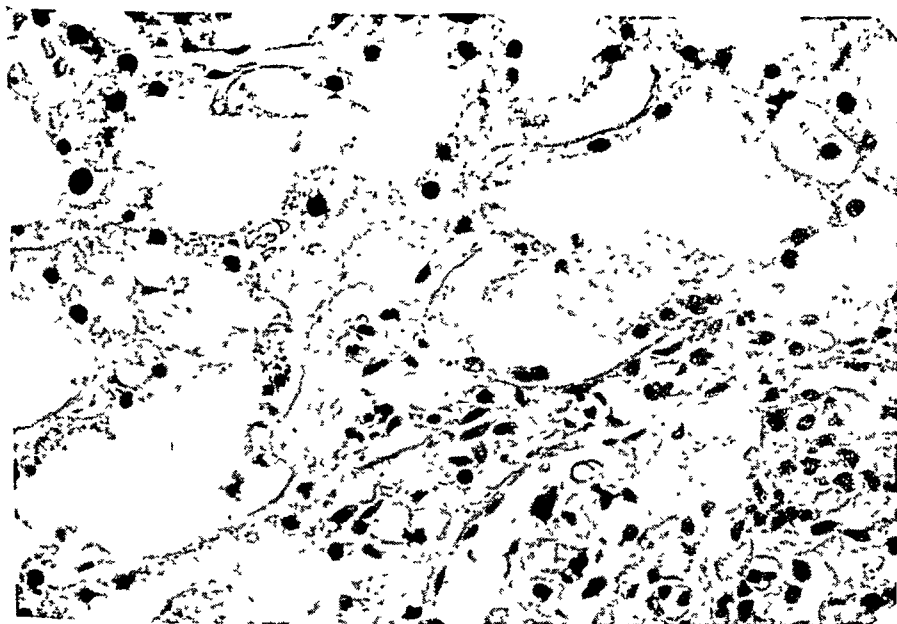


Fig. 14C (A. S., Case 44).—Kidney; complete loss of tubular epithelium; glomerulus intact ( $\times 700$ ).

turbance, and the histologic evidence of moderate degenerative changes has been found at autopsy (Fig. 13).

As the emphasis on liver damage as a possible explanation of the deaths during toxemia has receded, the importance of renal injury has received more attention. In two of the patients in the present series very severe oliguria developed with considerable rise in urea nitrogen.



Fig 15A (H. O.N., Case 45).—Kidney, essentially normal ( $\times 180$ ).

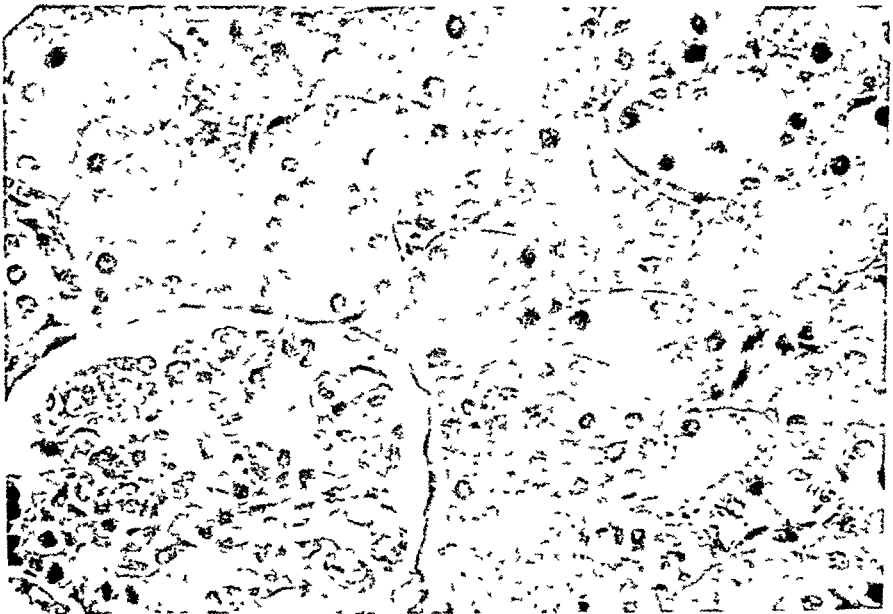


Fig 15B (H. O.N., Case 45).—Kidney; essentially normal ( $\times 700$ ).

Of the cases presented here in detail, three patients died within three to five days after receiving severe burns, with all the clinical evidence of severe toxemia. Post-mortem examination of these patients showed evidence of a toxic nephrosis with glomeruli intact but with marked degeneration of the entire tubule. The lining epithelium was necrotic and in many cases completely absent (Fig. 14). One patient (Case 19) died in renal failure. Sections of renal tissue from a patient dying fifteen minutes after receiving a third degree burn of 95 per cent of the body are included as controls for comparison with tissues of patients dying of burn toxemia (Fig. 15). These patients all showed the marked ganglion cell degeneration in the brain that was reported previously.<sup>39</sup>

In spite of the occurrence of oliguria, azotemia, and severe histologic changes in the kidney tubules, it does not appear that these patients died primarily of renal failure. The urea nitrogen did not reach the levels commonly seen in uremia, and in one of the patients with oliguria the daily urine volume had returned to normal before death. Furthermore, the urine output of nitrogen was increased in most instances after the burn, and the azotemia evidently developed in spite of increased nitrogen elimination. Moreover, the fractionation of the nonprotein nitrogen indicates that most of the azotemia was due to a rise in the undetermined fraction of the plasma nonprotein nitrogen.

In a few patients in the series the polypeptide fraction was determined by analyzing specimens for carboxyl nitrogen before and after phosphoric acid hydrolysis. The polypeptide fraction thus determined was elevated in rabbits as reported by Lambret and his associates.<sup>3, 4</sup>

The association between the clinical evidence of toxemia and the early rise in plasma undetermined nitrogen suggests that further investigation of the nature and origin of this fraction might be worth while. The substance or substances represented could be toxic or merely physiologically inert breakdown products resulting directly or indirectly from the lysis of the damaged tissues. Other experiments in this direction are in progress.

#### CONCLUSIONS

There was a marked rise in plasma nonprotein nitrogen within two to six days following thermal burns in seven patients. The rise in plasma nonprotein nitrogen was due chiefly to an increase in an as yet undetermined fraction.

The degree of this rise was of prognostic importance.

There was a constant but less marked increase in the excretion of urinary nonprotein nitrogen, with 30 to 50 per cent of the increase due to the undetermined fraction.

There was a considerable depression of the urea clearance during the phase of toxemia which persisted to some extent in cases of severe burns until the injured areas were epithelized. Since the occasional increase in blood urea nitrogen was not proportional to the rise in undetermined nitrogen, and since the urinary output was generally somewhat increased, it seems unlikely that kidney damage is the usual cause of death in burn toxemia.

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## SURGERY OF COLON AS SEEN IN AN OVERSEAS GENERAL HOSPITAL

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**S**URGERY of the colon as seen in a general hospital in Italy consisted chiefly of the care, closure, and treatment of colostomies which had been performed in the forward areas for large bowel perforations. There were only five original colostomies performed during this time by us, so the chief problem, aside from treating associated injuries, has been the selection and closure of colostomies suitable for closure in the time allotted for holding patients in an overseas theater. This report covers a period of thirteen months from Jan. 1, 1944, to Feb. 1, 1945, during which time 111 colostomies were seen, of which only 40 were closed.

There is no dispute concerning exteriorization of the injured large bowel. This is now a well-established principle, which was brought strongly to our attention by Ogilvie in his writings on the British campaign in Lybia. If the injured part of the large bowel cannot be exteriorized, then a proximal colostomy should be done. This also is an established principle which has produced excellent results.

As to the type of colostomy that should be done, there is still some controversy. Among the patients we have seen there have been many types of colostomies represented, ranging from the inefficient tube colostomy to the more radical double-barreled colostomy, with its limbs divided, and in some cases the stomata separated by skin. These extremes were rare, and for the most part colostomies have fallen into two classes, the spur and the loop. There are some who advocate the double-barreled spur type of colostomy, and contend that a loop colostomy will not completely shunt the fecal current from the distal bowel. On the other hand, we have found that the simple loop, when properly exteriorized, will completely shunt the fecal current. The loop colostomy can be done more easily, and at time of closure the continuity of the bowel can be restored more nearly to its original status. If it becomes necessary to resect a portion of the large bowel, then the double-barreled spur type is used. When this type of colostomy is performed, the spur should be clamped fairly early.

In the majority of the battle casualties in which there were large bowel injuries, the loop colostomy has been the method of choice because it is only temporary and is done in order to sidetrack the fecal current for four to eight weeks. In cases where there is only one perforation of the large bowel, this has occasionally been closed and exteriorized. In some cases of this type, it has not been necessary to open the loop and after eight to ten days to allow the healed perforation to retract into the peritoneal cavity. Most of these

patients will require a repair of the abdominal wall weakness at a later date, which is a simple procedure as compared with a colostomy closure.

All types of colostomies will have a tendency to retract during the first few weeks and the glass rod or tube placed under the loop will prevent this retraction and keep the posterior bowel wall level with the skin. If this is maintained for several weeks, and the colostomy opening is adequate, there will be no spillage of fecal material over into the lower bowel. It is best to open the bowel along its long axis, not necessarily in the longitudinal bands, and to have two-thirds of the incision on the oral side of the supporting rod. The mucosa will soon evert due to contraction of the circular musculature of the bowel. This type of incision is more readily closed and if the suture line is transverse to the bowel axis the closure will produce less constriction of the lumen.

As our experiences have dealt principally with the treatment of colostomies, we will deal chiefly with the treatment we have used pre- and postoperatively, the technique of closure, and supportive methods used in those colostomies unfit for closure in overseas theaters. Several which are representative of the types seen are also briefly reported.

After a patient with a colostomy has been admitted to a general hospital, and his case reviewed, one of the first questions that arises is when and where the colostomy should be closed. If the patient is debilitated and has other injuries which take priority over the colostomy, it may be best to return him to the Zone of Interior as soon as possible.

Of the 111 colostomies, 40 were closed. The reason for the colostomies is shown in Table I. The sites of injury are about equally divided over the large bowel, and closures are likewise equally divided among the sites of injury.

TABLE I. LOCATION OF INJURY WHICH NECESSITATED COLOSTOMY

	COLOSTOMIES CLOSED	COLOSTOMIES NOT CLOSED	TOTAL
Cecum	4	6	10
Ascending colon	4	5	9
Transverse colon	7	10	17
Descending colon	5	12	17
Sigmoid	5	13	18
Rectum	10	20	30
Perineal wounds	5	5	10
Total cases	40	71	111

The additional associated injuries are shown in Table II. Except for those patients who had paralysis of the major nerves, there seemed to be no one single injury which was thought to preclude closure before the patient was returned to the Zone of Interior. It was thought that the nerve lesion took priority over the colostomy and in these patients it was best to evacuate them as soon as they were in satisfactory condition, or to suture the nerve and leave the colostomy closure for a later period.

In Table III are given the complications which arose in addition to the injuries originally received. Infected abdominal wounds were the most fre-

TABLE II. ADDITIONAL ASSOCIATED INJURIES

	COLOSTOMIES CLOSED	COLOSTOMIES NOT CLOSED	TOTAL
Small bowel perforations	15	23	38
(single)	1	7	8
(multiple)	14	16	30
Bladder perforation	2	8	10
Spleen	1	4	5
Liver	2	4	6
Extensive soft tissue injuries	15	30	45
Chest and lung injuries	5	4	9
Paralysis of major nerves	0	5	5
Fractures	12	41	53
Ilium	3	8	11
Ischium	2	4	6
Pubis	0	2	2
Sacrum	1	10	11
Coccyx	1	3	4
Extremities	5	12	17
Skull	0	2	2
Amputations (major)	2	4	6
Arm	0	1	1
Thigh	0	1	1
Leg	2	2	4

quent single cause which prevented the closing of the colostomies. In all of these cases of infected wounds the colostomy had been brought out of the original abdominal incision, and not out of a small separate incision.

It is of interest to note, in view of the controversy concerning the cause of hepatitis and the possibility of transfusions of blood and plasma producing or being a contributing factor, that there was only one case of hepatitis in this series. All of these patients had multiple transfusions of both blood and plasma before and after admission to our hospital.

TABLE III. COMPLICATIONS

	COLOSTOMIES CLOSED	COLOSTOMIES NOT CLOSED	TOTAL
Pneumonia	1	8	9
Intestinal obstruction	2	5	7
Osteomyelitis of pelvic bones	0	8	8
Infected abdominal wounds			13
(original exploratory incision)	0	13	
Hepatitis	0	1	1

The mode of injury is shown in Table IV. As would be expected, shell fragments caused the greatest number of injuries, but even so twenty-five injuries from rifle or machine gun bullets seems high for this theater.

TABLE IV. MODE OF INJURY

	COLOSTOMIES CLOSED	COLOSTOMIES NOT CLOSED	TOTAL
Shell fragment	30	48	78
Bullet	7	18	25
Air bomb	0	3	3
Land mine	1	1	2
Hand grenade	0	1	1
Blast injury	1	0	1
Stab wound	1	0	1
Total	40	71	111



First, the complicating injuries must be treated. The soft tissue wounds are secondarily sutured or covered by skin graft, and the fractures treated according to their need. If there are open wounds near the colostomy which are continuously being contaminated, it may be necessary to close them at the time the colostomy is sutured, but all other wounds outside the area of constant contamination should be closed at the earliest possible time. Wounds of the iliac region and flank can often be closed and kept clean by appropriate dressings and care. In secondarily closing such wounds it is advisable to make a very loose closure with adequate space between each skin suture for drainage. Those patients who were in poor general condition or had other serious complicating wounds such as chest and lung injuries, destruction of the bladder, rectum, and anus, severe compound fractures, and laparotomy wound infections fall into the class where closure should be delayed. In those cases where time and condition allowed closure to be done in this theater, it was found that six weeks after the initial injury was an adequate interval to wait before closure, and in some cases closure could be done sooner. Immediately preoperatively the patients are put on a liquid diet for twenty-four hours. A rectal examination is done daily for three days preoperatively, and if any fecal material is found, an oil enema followed by a saline enema is given. Due to the great importance of having the lower bowel clean, the final check should be done by the surgeon himself. It might be added that fecal material is just as frequently found in the lower bowel when a double-barreled colostomy has been done as in the loop colostomy and most often it is not due to the spilling over of fecal material but was present in the lower bowel at the time of injury and had not been expelled or removed.

The colostomy should not be closed after division of the spur until edema of the mucosa has subsided, which usually takes several days. It should then be examined carefully to see that the spur has been cut down sufficiently and, if not, the spur should be further crushed.

Here again there is advantage in the loop colostomy, because there is no spur to be clamped with resulting edema, and consequently there is less chance of edema along the suture line at the time of closure, for it is well known that clamping the spur interferes with circulation of the bowel. There is also less chance of obstruction in a bowel that has the posterior part of the bowel wall left intact, especially that part along the mesentery attachments, as is the case in the loop colostomy.

The technical procedure carried out, with but few exceptions, in closing these colostomies is as follows: With the patient under nitrous oxide-ether anesthesia, the abdomen is prepared and draped, and the mucosal margins are then loosely closed with interrupted No. 00 chromic catgut sutures to prevent further soiling. The suture line should be transverse to the bowel axis to prevent constriction of the lumen. The abdominal skin is again cleansed and painted with iodine and alcohol and the patient completely draped. The surrounding tissues are first freed from the bowel down to the peritoneal cavity. The bowel closure is completed with two more rows of No. 00 chromic catgut,

the first of which is a continuous mattress stitch and the second a row of interrupted sutures. The two end sutures of this second row are left long and after the sutured colon has been placed back into the peritoneal cavity, they are passed through the peritoneum and tied so that the suture line of the bowel is held against the peritoneum, just beneath the wound. The peritoneum, muscle, and fascia are then closed in layers with interrupted chromic catgut. The skin is left unsutured and is drawn together on the fourth postoperative day with flamed adhesive.

Occasionally it has been found that this procedure would constrict the bowel lumen and before closure is begun an additional longitudinal incision was made in the bowel and then this enlarged stoma closed transversely. In these cases and in a few others it was necessary to open the peritoneal cavity before the mucosa was completely closed, and to free up both ends of the bowel. In two or three cases, where a double-barreled colostomy had been done, there was no hesitancy in doing a complete end-to-end anastomosis to insure an adequate bowel lumen.

Postoperatively we have used constant gastric and duodenal suction routinely for the first three days, during which time the patient is given 2,000 c.c. of 5 per cent dextrose in saline solution and one unit of plasma intravenously, daily. About the third day, when the patient usually begins to pass gas per rectum, the suction is discontinued, and clear fluids, cereals, and jellies are started by mouth. The diet is gradually increased until the tenth day, when the patient is placed on a regular diet provided there have been no complaints or discomfort after taking food. After the first week the patients are given 30 c.c. of mineral oil daily, and frequent rectal examinations are done to make sure that there is no accumulation of fecal material in the lower bowel. An oil enema is given whenever necessary. If these patients have no other complicating injuries, they are allowed to walk about the ward on the twelfth postoperative day.

In the patients in whom closures were done there were two who developed intestinal obstruction postoperatively. In both, simple catheter enterostomies were all that was necessary to relieve the obstruction, and both patients were back on a general diet within a few weeks. The enterostomy tubes were removed approximately ten days later and these wounds healed spontaneously. Only one of the colostomies which was closed developed a superficial wound infection which cleared up readily and did not prolong the period of hospitalization. In one other case the wound broke open, and there was a small amount of fecal drainage for several days, after which it closed spontaneously. This was the only case in which a ventral hernia developed, requiring repair at a later date. There were no deaths among the 111 colostomy cases, and no evidence of peritonitis was found in any of the 40 patients after the closure operation.

Five brief reports of typical cases are given here. The first three are cases in which closure was not done; the reason for the delay in closure is quite obvious in each case. In the last two cases closure was done and the

patients have had no further symptoms after being evacuated. One (Case 4) of the two had a postoperative obstruction caused by extensive edema at the suture line which was produced by enfolding excessive mucosa at the time of closure as the colostomy opening was quite large (see Fig. 4).

#### CASE REPORTS

**CASE 1 (Fig. 1).**—A soldier wounded in action by enemy shell fragments on Aug. 26, 1944, near Cleon, France, sustained a severe penetrating wound of the abdominal cavity with perforations of the stomach and transverse colon. Débridement of the wound of entrance, which was in the midaxillary line between the tenth and eleventh ribs, removal of foreign body, closure of the gastric perforation, and a double-barreled colostomy in the transverse colon were done on the day of injury at an evacuation hospital. This patient was admitted to the Forty-fifth General Hospital on Sept. 2, 1944, at which time he was markedly dehydrated and in poor general condition. It was also noted on admission that

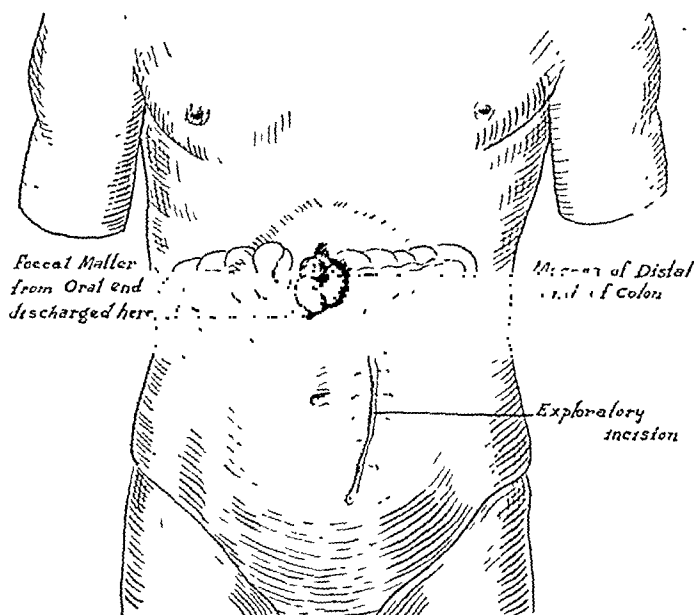


Fig. 1 (Case 1).—Proximal limb of colostomy has retracted; an intraperitoneal abscess developed which drained both through the bowel and around the colostomy.

the proximal exteriorized portion of the colon was gangrenous and sloughing. For the next twelve hours after admission his condition became progressively worse, his abdomen distended and aperistaltic. After forty-eight hours, during which time he was given intravenous fluids and blood transfusions, and constant gastric suction was maintained, his general condition improved and he began to pass a small amount of gas and liquid feces through the colostomy. From this time on his condition became steadily better. He later developed a left pleural effusion, for which multiple chest aspirations were done, and an intra-abdominal abscess, which drained spontaneously through the mid-portion of the laparotomy incision and from the lumen of the distal limb of the colostomy. This drainage ceased spontaneously and his condition became suitable for evacuation to the Zone of Interior on Oct. 16, 1944.

In this case several months' convalescence was necessary before closure of the colostomy could be attempted. A spur type of colostomy was done, but

there was too much tension on the proximal end and also an inadequate blood supply. Several inches of the bowel sloughed and the entire colostomy retracted, from which infection of the wound developed and also an intraperitoneal abscess. In this case it would have been better to have brought the ends of the bowel out of separate wounds or to have freed up more of the bowel before forming a spur.

CASE 2.—A patient wounded in action by enemy shell fragments Aug. 26, 1944, near Alex, France, sustained three perforations of the jejunum and severe damage to the splenic flexure of the colon. The perforations of the jejunum were closed, the splenic flexure of the colon resected, and a spur colostomy done in a field hospital on the day of injury. On the fifth postoperative day the patient developed signs of a right subphrenic abscess which was drained transabdominally, just below the costal margin in the anterior axillary line, and about 800 c.c. of purulent bile-stained material was obtained. It was

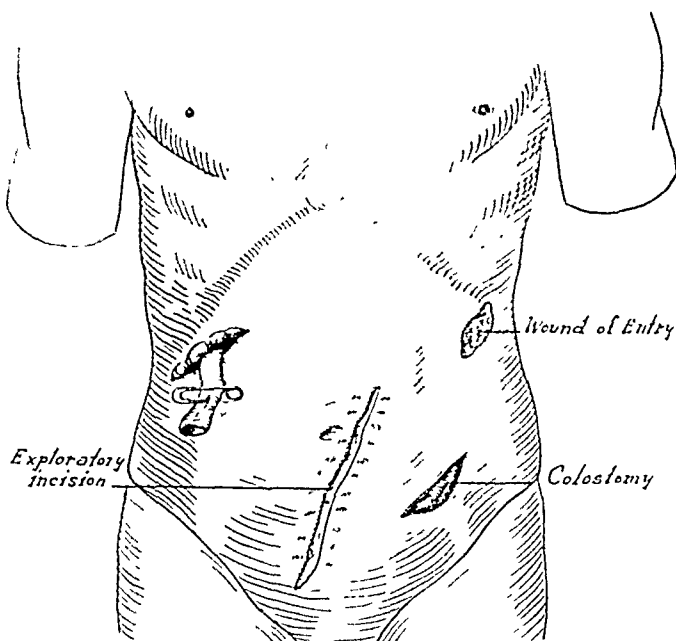


Fig. 2 (Case 2).—The drain is shown in the subdiaphragmatic abscess which later developed into a duodenal fistula. There was also an acute obstruction of the lower portion of the small bowel. Due to the recent duodenal fistula and intestinal obstruction the patient was evacuated without closure of the colostomy.

noted on the following day that duodenal contents were draining from the abscess cavity. On admission to the Forty-fifth General Hospital on Sept. 18, 1944, the patient showed marked excoriation of the abdominal wall and on the first day after admission there was 1,800 c.c. of duodenal drainage. Continuous suction was used to keep the wound dry and the duodenal fistula gradually closed spontaneously. On Oct. 27, 1944, the patient developed an acute intestinal obstruction which was found to be in the lower small bowel and caused by adhesive bands. After release of these adhesions the postoperative course was uneventful and he was returned to the Zone of Interior on Nov. 29, 1944 (see Fig. 2).

In addition to the abdominal injuries, he had a severe wound of the left leg with compound, comminuted fracture of the fibula. After the duodenal fistula had healed and the blood picture had been brought up to normal, the leg wound was closed by suture and split-skin grafts. After his return home, the colostomy was successfully closed.

Closure in this patient and also the patient in Case 1 could have been done overseas, but it is felt that colostomies with definite intraperitoneal or abdominal wall infection are best closed three or more months after injury and therefore evacuation to the Zone of Interior is advisable as soon as the infection has been cleared up and the general condition permits.

CASE 3.—A soldier wounded in action by an enemy land mine Aug. 31, 1944, near St. Maxine, France, sustained three perforations of the ileum, a perforation of the rectum, a lacerated spleen, and a compound fracture of the right femur. The three perforations of the ileum and the perforations of the rectum were sutured along with a splenectomy and a loop colostomy of the sigmoid at an evacuation hospital on the day of injury. On Sept. 4, 1944, the thigh wound was débrided and the fractured femur was fixed with three vitallium screws. The patient was admitted to the Forty-fifth General Hospital on Sept.

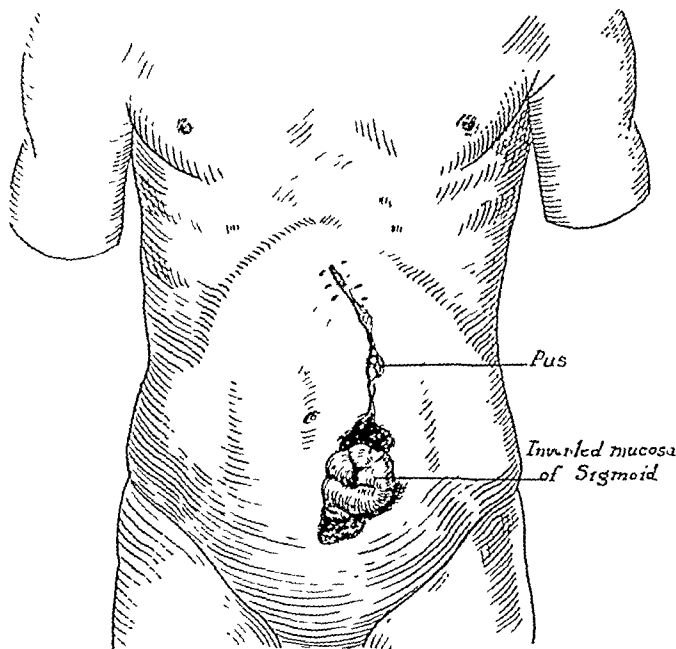


Fig. 3 (Case 3).—This patient developed a large intra-abdominal abscess which drained through the mid-portion of the laparotomy incision. It would have been better to have brought the colostomy out of a separate incision. This patient also had a severely compound comminuted fracture of the right femur.

13, 1944, in poor condition. A septic course continued, with signs of an intra-abdominal abscess. On Oct. 5, 1944, the upper end of the incision was probed and a large amount of thick yellow pus obtained. After drainage of the abscess he improved steadily and on Nov. 7, 1944, his condition became suitable for evacuation to the Zone of Interior. The infection of the abdominal wound and resultant intraabdominal abscess can be partially, if not wholly, attributed to the colostomy being made in the original abdominal incision, as the infection was first noted there and seemed to spread downward. A colostomy through the original laparotomy incision in battle casualties should be avoided if possible (see Fig. 3).

CASE 4.—A soldier wounded by enemy mortar shell July 17, 1944, near Palaia, Italy, sustained three perforations of the splenic flexure of the colon which were exteriorized as a loop colostomy through a stab wound in the upper left quadrant of the abdomen. He

was admitted to the Forty-fifth General Hospital on Sept. 22, 1944, in good condition. On Oct. 11, 1944, the colostomy was closed. He developed an obstruction on the ninth postoperative day, for which an enterostomy was done. The patient showed no further signs of obstruction. On Nov. 14, 1944, he was returned to the Zone of Interior, at which time he was ambulatory and eating a regular diet (see Fig. 4).

This colostomy is one of the type which we believe should be closed in an overseas theater, although the patient was one of the two who developed an obstruction following colostomy closure. He became transportable before the expiration of the time limit of hospitalization in this theater. Several months later he reported that he was in excellent health and had had no further trouble or complaints.

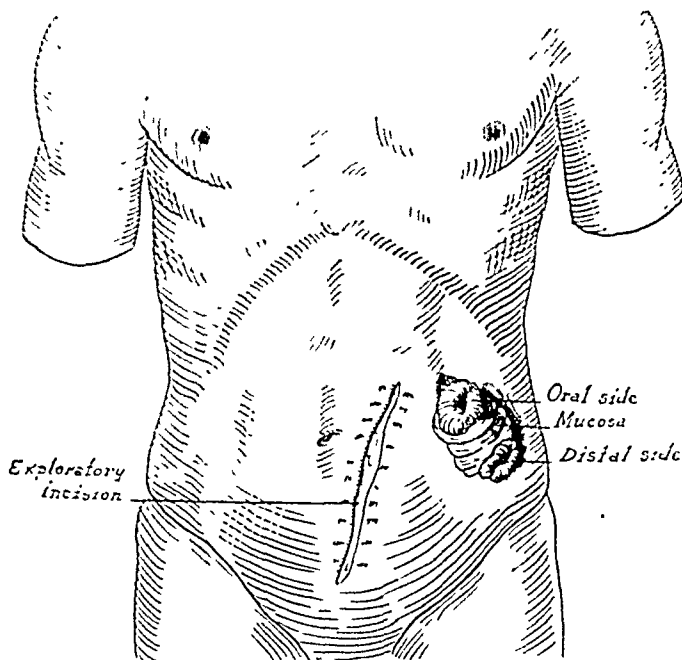


Fig. 4 (Case 4).—Much of the mucosa of the anterior part of the bowel was destroyed at the time of the original injury. The mucosa was greatly everted and edematous, but there was no spillage of fecal material into the lower bowel.

CASE 5.—An officer wounded in action by shell fragments on May 15, 1944, near Madrogone, Italy, received a severe penetrating wound of the left iliac region. The shell fragment produced a shattering fracture of the left ilium and penetrated the sigmoid. The wounds were débrided on the day of injury at an evacuation hospital and the injured bowel was exteriorized as a loop colostomy. Eight days later the patient was transferred to the Forty-fifth General Hospital where he was received in good condition except for being slightly anemic. He was given two blood transfusions of 500 c.c. each on successive days, and two days later, twelve days after his original injury, the soft tissue wounds were closed. Adhesive strips and dressings were placed in such a manner as to prevent soiling of the wound in the iliac region from the colostomy. The soft tissue wounds healed rapidly and satisfactorily.

Five weeks after the original injury the colostomy was closed and the patient made a normal and satisfactory recovery. Four weeks later, after being ambulant about the ward for several days, he was transferred to the Zone of Interior. Four months after the original injury he wrote that he had been reassigned to duty and had had no further trouble.

Closure was easy in this patient but is of interest because of the wound in the region of the left ileum which was being constantly contaminated by the drainage from the colostomy, and with a little extra care the wound was sutured and healed readily. All concomitant wounds in these cases should be closed as soon as the patient's condition permits.

#### SUMMARY

1. A brief summary has been given of 111 colostomy cases in an overseas general hospital.

2. Treatment consisted of supportive measures, closure of associated soft tissue wounds and reduction of fractures, and the closure of many of these colostomies. There were no deaths in the entire series of 111 cases and 40 of the colostomies were closed. Postoperatively there was fecal drainage in only one patient, which cleared up spontaneously within ten days.

3. In injuries to the rectum and lower sigmoid the loop colostomy is adequate and preferable.

4. Exteriorization of the injured part of the bowel by loop colostomy is advised. If the perforation is small, suture of the perforation and exteriorization without opening the bowel lumen, should be done.

5. The colostomy should always be brought out through a small, separate abdominal incision, preferably away from the lower rib margins.

6. Closure of colostomies should not be attempted in an overseas theater in the presence of wound sepsis or if obvious peritonitis has existed within six or eight weeks.

7. No closure should be attempted until all plastic work on the lower bowel, anal sphincter, urinary bladder, or perineum have been completed.

# Review of Recent Meetings

## THE FIFTY-SEVENTH ANNUAL MEETING OF THE SOUTHERN SURGICAL ASSOCIATION

HOT SPRINGS, VA., DEC. 4-6, 1945  
GEORGE D. LILLY, M.D., MIAMI, FLA.

THE members of the Southern Surgical Association were the guests, December 3, of Brigadier General Clyde M. Beck and Colonel Daniel C. Elkin and the Medical Staff at The Ashford General Hospital. During the morning a scientific program was presented. Captain William H. Galvin discussed Anesthesia for Operations of Long Duration. Captain William C. Ward and Major George C. Prather outlined their Treatment of the Paralyzed Patient. Major William B. Patton described the Treatment of Pulsating Exophthalmos. Major Ernest G. DeBakey reported his experience with Repair of Extensive Nerve Defects.

There was a symposium of Unusual Problems in Bone Replacement. Captain Louis M. Rosati discussed Bridging of Defects of the Femur. Captain Edmond R. Zaglio described a Deformity of the Radius Due to Aneurysm. And Major Hugh H. Trout, Jr., described The Repair of Skin Grafted Bone Cavities.

Captain Fred W. Cooper, Jr., discussed Resection of the Clavicle for Certain Vascular Lesions. Major M. H. Harris considered the diagnosis and management of Arteriovenous Aneurysms of the Vertebral Vessels. Captain Jacob W. Kahn described the Effect of Atropine on Branham's Sign. And James V. Warren considered The Effect on the Circulation of an Arteriovenous Fistula.

The fifty-seventh annual session of the Southern Surgical Association was held at the Homestead Hotel, Hot Springs, Va., on December 4, 5, and 6, 1945.

Charles A. Vance presided and Alfred Blalock served as secretary. I. A. Bigger was chairman of the committee on arrangements.

William P. Longmire began the scientific program by describing A New Method for Constructing an Artificial Esophagus. He reviewed the medical literature on this most interesting subject, and then described a procedure employed by himself and Mark M. Ravitch on three patients. A long segment of proximal jejunum with a single arterial loop blood supply was isolated and the continuity of the intestinal tract was re-established. This isolated loop was then brought out upon the abdominal wall through a stab wound and was used as the inner lining of a long skin tube which was made from the integument of the anterior abdominal wall. In a short time the isolated segment of bowel had begun to derive its blood supply from the enveloping skin tube, and it became possible to sever its intra-abdominal blood supply. This created a typical tube flap which was then "walked" into place on the anterior thorax so that it could be attached to the cervical esophagus above and to the stomach below. Such a tube, with its intestinal lining, has the advantage of a mucosal lining naturally adapted to its function, and swallowing is expedited by normal peristalsis which occurs in this type of tube. A motion picture was shown to demonstrate the normal peristalsis in the tube after the operation was completed.

Champ Lyons presented the results of his Investigation of Chemotherapy in Wound Management in the Mediterranean Theatre. Lyons stressed the point that no chemotherapy is of value in the prevention of toxemia caused by the absorption of the products of tissue

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decomposition which occurs in wounds not properly débrided. The antibacterial potency of various drugs was studied on microorganisms which were divided into three categories: true pathogens, wound pathogens, and commensal organisms. Lyons concluded that the local application of sulfonamides is definitely injurious. He advocated thorough débridement (not "wound trimming"), proper wound splinting, and the systemic use of the proper drug for the particular pathogens encountered.

Major Robert P. Kelly discussed the experiences which he and his colleagues, Captain Louis M. Rosati and Captain Robert A. Murray had had with **The Treatment of Traumatic Osteomyelitis**. They advocated early excision of the diseased tissue with a temporary covering by means of a dermatome graft. This temporary repair could be followed by a pedicle graft at a later date.

Walter C. G. Kirchner outlined his method for **The Treatment of Chronic Osteomyelitis and Deep-Seated Infections by the Employment of an Epithelized Sinus or Drainage Channel**. He pointed out that such infections were cleared up most readily when open drainage was effected. To accomplish this, he advocated the creation of channels down to the site of infection. By keeping these channels open with dilators, he allowed the contiguous epithelium to grow down into the drainage tract. He found that these epithelial-lined drainage channels assured direct, prolonged drainage, and relieved tension. He has found that as the healing process takes place the channel closes.

Guy A. Caldwell presented his method for **The Repair of Bone Defects Associated With Chronic Osteomyelitis**. He advocated the removal of all scar tissue and ebonated bone to the extent that all remaining tissue had a healthy blood supply. He then employed muscle grafts to fill the cavities and these were, in turn, covered by skin. In twenty-one cases of localized osteomyelitis treated by this method, 81 per cent healed per primam, and 63 per cent remained healed. In twenty-two cases of hematogenous osteomyelitis, 81 per cent healed per primam and 63 per cent remained healed for a period of observation ranging from five to twelve months. Caldwell gave a clear description of the pathology involved in osteomyelitis, and pointed out the necessity of removing all infected tissue and scar, as well as all sclerosed bone.

George D. Lilly advocated lumbar sympathetic ganglionectomy as a preliminary procedure before doing an obliterative endo-aneurysmorrhaphy upon **Aneurysms of the Lower Extremity**. He explained that sympathectomy was a quick and efficient method of establishing adequate collateral blood supply to an extremity, even in individuals with advanced arteriosclerosis. He reported four cases in which major vessels had been occluded in elderly people with no evidence of impaired circulation or function.

Colonel D. C. Elkin discussed **Cirroid Aneurysms**. He called attention to the fact that trauma to a pre-existing telangiectatic area frequently is the cause of cirroid aneurysms. For this reason, such lesions have been observed more frequently during wars. Several personal cases were presented and their treatment described. Elkins has found that in treating this type of lesion in the scalp, the best results can be obtained by ligating the superficial temporal artery, turning down a scalp flap, opening the galea, and excising the vascular mass from the underside. He illustrated excellent results from the use of this method.

John J. Pemberton reported a case of **Traumatic Arteriovenous Fistula Involving the Abdominal Aorta and the Vena Cava**. With the assistance of Philip H. Seefeld and Nelson W. Barker he was able to repair this defect by a transvenous approach. The patient was a 28-year-old man, who had received a gunshot wound seven years previously. Hemostasis was obtained by digital compression of the aorta, and the fistula was sutured with silk. This is the first successful case of this type to be reported.

Lieutenant Colonel Michael E. DeBakey analyzed the incidence and results of 2,453 Vascular Injuries in the United States Army During World War II. DeBakey's study contains a wealth of statistical data which will be of great value in further studies pertaining to vascular injuries in warfare.

A Symposium dealing with the Newer Concepts in the Treatment of the Paralyzed Patient Due to Wartime Injuries of the Spinal Cord was presented by a group of Army surgeons.

Colonel David H. Poer outlined a plan for the management of this type of case and described the results of nutritional studies. Poer reported that there were 13,000 such cases in the Army. His group had had seventy-seven cases at the Newton D. Baker Hospital, and in this series one-fifth of the injuries were in the cervical region, 30 per cent were in the cauda equina, 38 per cent were complete, and 62 per cent were incomplete. When these patients were admitted to general hospitals, 74 per cent had developed emaciation with an average weight loss of forty pounds. Most of them had secondary anemia, and 46 per cent were in negative nitrogen balance; 57 per cent had decubitus ulcers. In accordance with specific Army regulations, all of them had had suprapubic cystotomies done; 57 per cent had had laminectomies. In his series there was one death. Each of his seventy-six remaining patients was able to sit in a chair within one month after admission.

Lieutenant Colonel Charles W. Elkins and Major Walter R. Wegner described the neurosurgical management of these patients. Twelve still had foreign bodies in the spine. These were removed. There was no evidence of improvement after the removal, but the patients did not get any worse. It was felt that the formation of additional scar tissue was avoided by removing the foreign bodies. Many patients were subjected to operation because of pain. Spinothalamic caudotomy was of value. A great deal of difficulty was experienced with uncontrollable spinal reflexes. He classified these reflexes as being flexion, extension, reflex stepping, and crossed reflexes. They found that the level of the injury had no bearing upon the nature of these reflexes, except that cauda equina lesions were always flaccid. They found that extensor reflexes were frequent in incomplete lesions. They employed anterior rhizotomy in some of the more severe cases.

Major Boris P. Petroff discussed the use of Streptomycin in the Treatment of Urinary Infections in Paralyzed Patients. He advocated the surgical treatment of calculi and abscesses, and found that streptomycin was of great value in the treatment of some of the more prevalent gram-negative bacilli infections. He found that some of these organisms developed resistance to streptomycin, but their pathogenicity was reduced by the drug.

Captain Donald E. Barker discussed these seventy-seven cases from the standpoint of the plastic surgeon. He found that decubitus ulcers were a major problem, and described his technique for repairing them.

Admiral Winchell M. Craig, in discussing these presentations, stated that the Navy was doing a transurethral resection of the internal sphincter of the bladder with good results in many cases of paralysis.

Captain Robert L. Payne, Jr., and Captain Darrel Shaw described The Repair of Surface Defects of the Upper Extremity. They stressed the importance of repairing skin defects first and then repairing injuries to the bone, tendons, and nerves after healing had taken place. They made extensive use of abdominal skin flaps and stressed the importance of accurate and complete closure of all tube flaps, in order to avoid infection. Photographs of many patients were used in demonstrating technique and exhibiting results.

Lieutenant Colonel T. G. Blocker described The Use of Cancellous Bone in the Repair of Defects About the Jaws. He called attention to the great increase in the incidence of bony injuries of the face and jaws in World War II, as compared with World War I, and advocated the use of pure cancellous bone from the ileum in repairing such defects because he has found that the rate of bony regeneration is inversely proportioned to the density of the bone used. He described the use of this material in 457 injuries.

John Staige Davis compared Plastic Surgery in World War I and World War II. He found that no new principles had been devised in either war, but that the vast abundance of clinical material enable plastic surgeons to improve and perfect their technique. He found that military organization for adequate, competent treatment by well-trained experts working in highly specialized centers had made this work much more valuable in World War II. He pointed out that the attention paid to psychologic problems in plastic surgery problems in this war had been of great value.

Charles S. Venable and Walter G. Stuck advocated Muscle Implant in the Treatment of Non-articular Hypertrophic Arthritis of the Hip. The clinical picture and pathology of aseptic necrosis of the head of the femur was described, and their method of cutting a slot in the front surface of the greater trochanter and neck of the involved femur was illustrated. A muscle flap from the vastus lateralis was transferred into this bony slot. They believe this establishes a new blood supply to the ischemic bone. In twenty-six of their twenty-seven cases, all pain was relieved.

Albert Key discussed the use of Bunnell's Pull-Out Wire Sutures for the Fixation of Tendons. He illustrated the use of stainless steel wire as a pull-out suture, as first described by Bunnell in 1934. He believes that this method has a great advantage in tendon suture because the suture material is strong, flexible, and can be removed in four weeks leaving no foreign body in the tendon.

William H. Prioleau described Muscle Flap Closure of Cavities Resulting From Lung Abscesses. He felt that such procedures should be carried out in multiple stages. Catheter drainage should be employed, the remaining cavity should be unroofed, then the residual cavity and the associated bronchial fistula should be closed by transplantation of muscle flaps. Nine personal cases were described.

Lieutenant Colonel Brian Blades reported The Cases of Mediastinal Tumors Treated at Army Thoracic Surgery Centers in the United States. Of the 107 cases studied, 23 were bronchogenic mediastinal cysts; 17 were benign teratomas; 6 were tumors of thymic origin; 21 were benign neurogliomas; 1 was a malignant neurosarcoma; 7 were unclassified cysts; 1 was a thyroid adenoma; 1 was a tuberculoma; 3 were Hodgkin's granuloma. In this series there were no operative deaths. Blades feels that opening the chest to establish definite microscopic diagnosis is a safe and justifiable procedure. He does not approve of the use of x-ray therapy as a therapeutic test.

Isidore Cohn read a paper on Dyschondroplasia. The embryology and clinical picture of this hereditary developmental disease was described, and several cases from a single family were presented.

Donald Guthrie and Gerard Gagnon discussed The Prevention and Treatment of Post-operative Lymphedema of the Arm. They reviewed a series of 100 breast operations, in which 46 patients had axillary metastasis. In this series there were 8 patients with lymphedema, treated by the subcutaneous insertion of celloidin strips. These were left in place for from five to six weeks and they seemed to aid in the development of new lymph channels. There was a marked improvement in the lymphedema of the arm.

Francis M. Massie advocated Refrigeration Anesthesia for amputations. He pointed out that with refrigeration, amputations can be deferred indefinitely until the patient can be properly prepared for surgery. A motion picture was shown to illustrate the use of this method.

Colonel R. Glen Spurling and Lieutenant Colonel Barnes Woodhall described their Experiences With Early Surgery in Peripheral Nerve Injuries. Seven thousand end-to-end nerve sutures have already been reported in World War II. It is too soon to evaluate the final results, but it would appear that the best results are obtained when repair is carried out within three weeks after injury. In this series 91 per cent showed some evidence of regeneration.

Cobb Pilcher described the Radical Extirpation of Vascular Malformations of the Brain. He explained that removal of such lesions had always been looked upon with disfavor because of the poor results. He believes, however, that if lesions are small and localized, and the symptoms are severe, operation is indicated. Three successful cases were presented.

Ernest Sachs presented an Analysis of Brain Abscesses Observed in the Past Thirty Years. His series contained 142 cases; 128 of these patients were operated upon and 59 of them were cured. He advocated conservative treatment until a capsule is formed, and then complete excision.

Edgar F. Fincher also advocated The Surgical Treatment of Brain Abscess by Complete Removal. He presented five personal cases showing the value of this procedure.

J. M. Emmett and M. L. Dreyfuss discussed Malignant Tumors of the Small Bowel. The literature of this subject was reviewed, and two personal cases were reported.

Howard Mahorner described a plan for Restoration of Continuity After Resection of the Rectum. He pointed out that a satisfactory anterior resection with restoration of continuity can be carried out when the lesion is 8 cm. or more above the anal orifice. For those at a lower level he advocated their removal through a posterior oblique incision following mobilization from above.

Robert L. Rhodes presented Further Observations Upon Imperforate Anus. He observed that about 500 infants with this abnormality are born in the United States each year. Rhodes pointed out that such a condition is not an emergency procedure in the newborn infant, because the bowel content is relatively sterile. He advocated a twenty-four to forty-eight hour delay, and then x-ray in an inverted position. This affords a good visualization of the lower bowel. Surgical repair can be undertaken with considerable ease. Four personal cases were reported.

Frank S. Johns discussed Defects of the Abdominal Wall in the Newborn. The embryology was reviewed and the medical literature was analyzed. His own successful case was described in detail.

R. L. Sanders considered The Indication and Value of Choledochoduodenostomy. He reported 25 personal cases, 16 of the patients alive and well from one to twenty-five years after surgery, with no evidence of infection.

Vernon C. David described his Experiences in Subtotal Resection of the Pancreas for Hypoglycaemia. When such patients were operated upon and no tumor was found, a subtotal resection was done. Thirty-six cases were reviewed; 63 per cent of the patients were cured, 31 per cent were improved, and 6 per cent died.

E. Dunbar Newell reported Forty-Eight Consecutive Cases of Gangrenous Suppurative Appendicitis With Removal of the Appendix and Complete Closure of the Wound Without a Death.

Guy L. Hunner asked the question, Is Urethral Stricture an Etiological Factor in the Genesis of Renal Tumor? He reported several cases of kidney tumor associated with urethral strictures.

Dr. William E. Lower will publish A Clinical Report of Cases of Urethral Transplantation Done More Than Fifteen Years Ago.

Frank W. Smythe discussed Malignancies of the Female External Genitalia.

W. O. Bullock advocated Vertical Traction: An Aid in the Surgical Management of Certain Massive Tumors. Bullock described a most interesting case of an enormous neurofibroma in which overhead pulley traction was used. An illustrative moving picture was shown.

Joseph A. Danna described The Treatment of Sebaceous Cyst by Electrosurgical Marsupialization. He advocated fulgurating the skin over the cyst in a small area and then allowing the cyst to drain.

# FIRST GENERAL MEDICAL MEETING AT DE WITT GENERAL HOSPITAL

LIEUTENANT COLONEL AMBROSE H. STORCK,\* MEDICAL CORPS,  
ARMY OF THE UNITED STATES

THE First General Medical Meeting at De Witt General Hospital, Auburn, Calif., was held Sept. 14 and 15, 1945. This hospital is a vascular center and a neurosurgical center and, in addition, has active general surgical, orthopedic, and other surgical sections. Major Donald C. Malcolm acted as chairman and introduced the speakers. A total of forty-one subjects were presented by guest speakers and members of the hospital staff. The material presented by members of the De Witt staff was based chiefly on recent work and observations. Abstracts of the thirty-five presentations which were of surgical significance are given in this report.

**Lieutenant Colonel Ambrose H. Storck, De Witt General Hospital. Organization and Operation of a Vascular Center.**—The vascular center at De Witt General Hospital is one of three such centers established to furnish highly organized facilities for the study and treatment of diseases and injuries of the vascular system, particularly the peripheral blood vessels, occurring in both Zone of Interior and overseas casualties. In order to accomplish the intended purpose, medical officers equipped by training and experience in the investigation and management of vascular disorders were assigned to the staff. Nurses and technicians were trained locally to meet the special requirements. The center is composed of a surgical vascular section and a medical vascular section. Directly admitted to the surgical section are those patients with lesions which will likely require operative procedures, including arterial aneurysms, arteriovenous fistulas, gangrenous and other open lesions of vascular origin, varicose veins, hemangiomas, and patients with acute venous thrombosis. Patients admitted initially to the medical section include those with nonulcerative vasospastic and obliterative arterial disease, peripheral edema, and chronic thrombophlebitis. Ward rounds and conferences on both surgical and medical sections, attended by all concerned personnel, provide for exchange of thought and afford frequent opportunities for selecting patients to be transferred from one section to the other.

A dry clinic conducted once a month serves as a means of presenting to all interested members of the hospital staff the newer developments and the work in progress in the field of vascular lesions. A weekly "neurovascular" conference is held with members of the neurosurgical section for the purpose of considering cases and problems of combined vascular and neurologic interest.

A constant temperature room, skin-temperature recording apparatus and other appropriate recording apparatus, and special supplies required in the study of vascular disease are available. Operating room special equipment includes pneumatic tourniquets; Bethune tourniquets threaded and padded with split rubber tubing, for direct arterial compression; a manometer for directly measuring intra-aneurysmal and intravascular pressure; a sterile stethoscope for auscultation during operation; and special dissectors, forceps, and lights. Two oscillating beds have been used to advantage on several occasions, both before and after operation.

A total of 1,269 patients had been admitted to the vascular center by Sept. 1, 1945, and up to that time 258 operations had been performed, including 70 for aneurysms and arteriovenous fistulas, 50 sympathectomies, 54 vein ligations, and 37 toe amputations in trench foot cases. There have been no deaths, and no instance of postoperative gangrene, the latter result being attributable to the attention which has been given to the study, development, and maintenance of collateral circulation. No mechanical anastomosis

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devices have been used. Experiences at this center have demonstrated a more than usually accepted possibility of restorative suture and preservation of the continuity of both arteries and veins involved in aneurysms and arteriovenous fistulas. Simultaneous ligation of veins accompanying arteries which must be ligated or otherwise occluded has not been a practice. When feasible, arteries have been ligated just beyond the nearest proximal branch. The success with which restoration of arteries and veins can be accomplished without subsequent thrombosis, even though no anticoagulants are used, has been striking.

In addition to the main purpose which this vascular center has served in caring for patients, the training of medical officers who previously were only slightly acquainted with the management of vascular problems has been a very important by-product. Familiarity with methods of examination and treatment in vascular diseases was gained by those regularly assigned staff officers who were rotated through the various sections of the surgical service, instruction was given to temporarily assigned recent medical school graduates who had just completed their training at the Medical Field Service School at Carlisle Barracks, and refresher type training was provided for medical officers from other stations who were temporarily assigned to De Witt General Hospital. At least three medical officers have, as a result of their training and experience here, been developed to the point where they are capable of caring for complicated vascular lesions and of independently performing major vascular operations.

In addition to clinical observation in cases in which the various practices already referred to have been followed, special investigative work has been done on basal vascular tone and studies have been conducted on collateral circulation by a fluorescein-ultraviolet light method.

**Major John W. Waller, De Witt General Hospital: Obliterative Peripheral Vascular Disease.**—Discussion of the incidence, diagnosis, and treatment of arterial obliterative lesions was given to show that arteriosclerosis obliterans and Buerger's disease are relatively common, that they can be diagnosed in their early stages by simple clinical methods, and that they are amenable to therapy. Arteriosclerotic disease of the extremities has been found in many young people between the ages of 20 and 40 years, and is occurring with increasing frequency in the general population. Buerger's disease is more common than has been suspected, with a large group occurring in the late forties. Intermittent claudication is diagnostic of arterial insufficiency. Sudden onset of coldness with pallor is very suggestive. Superficial phlebitis usually means Buerger's disease. Physical examination of the pulses is easy and helpful. Reactive hyperemia test for small blood vessel obliteration was described. Diagnosis of Buerger's disease rests on uneven distribution of the arterial lesion and the presence of superficial migrating phlebitis. The wide racial distribution with no predilection was shown statistically.

Patients with Buerger's disease must stop smoking. If the limb is cold, sympathectomy will help. If surgery is contraindicated, intravenous typhoid vaccine therapy is used. In any obliterative arterial disease the care of the feet is most important and the body should be kept warm to prevent vasoconstriction.

**Captain T. B. Massell, De Witt General Hospital: New Method for Testing Collateral Circulation.**—Before ligating a major artery at the time of operation for excision of traumatic aneurysm, it is necessary to be sure that there is adequate collateral circulation. Clinical observation and the location of the lesion give some clue to the state of collateral blood supply, but a more definite test is necessary.

The collateral circulation test based on the time of color return after compression with an Esmarch bandage has been used, but has been found to give variable results. Consequently, a new test for collateral circulation has been devised, based on Neller and Schmidt's wheal fluorescence. With the aneurysm tightly occluded by a Matas clamp, a series of parallel scratches about 8 cm. apart is made both on the involved extremity and on the one opposite. Ten cubic centimeters of 10 per cent of fluorescein are injected

into an arm vein and the level of wheal fluorescence is examined by filtered ultraviolet light. With adequate collateral circulation, the lowest level of fluorescence on the involved extremity should be not more than 8 cm. higher than on the normal extremity.

Twenty-three patients with traumatic aneurysms have been examined by this technique. Sixteen have had operative excision of the aneurysm, four have had plastic restoration of the artery involved, and twelve have had ligation. Nine patients with arteriovenous aneurysm and one with a simple arterial aneurysm had good collateral circulation before operation, both by the fluorescein wheal and the ordinary collateral circulation test. Four of these had inadequate collateral supply by one or both tests when first observed. All four had lumbar sympathectomy performed, following which the collateral circulation became adequate.

Two patients had inadequate collateral circulation by the fluorescein wheal and ordinary tests but, at the time of operation, in each case a large arterial branch which had been occluded by the Matas clamp in performing the examination was found close to the aneurysm.

On the basis of these preliminary studies, wheal fluorescence seems a somewhat more reliable test for collateral circulation than the older collateral time test.

**Lieutenant E. W. Rector, De Witt General Hospital: Basal Vascular Tone as an Indication for Sympathectomy.**—The need for adequate collateral blood supply in surgical lesions of arteries and the advantages of sympathectomy as an adjunct to surgical procedures on the vessels were discussed. Reference was made to Naide's method of determining basal vascular tone, and the method was described in detail. An attempt was made to evaluate this test as a criterion for sympathectomy. Patients showing high vascular tone were considered suitable for sympathectomy since they were least apt to develop an adequate collateral supply without this procedure. Marked improvement in the development of collateral circulation after sympathectomy was noted in patients with arterial lesions.

Six of seven patients with Raynaud's disease on whom the basal vascular tone was determined had high tones. Out of thirteen patients with trench foot, nine showed high tones. In twenty-two cases of Buerger's disease, fourteen had high vascular tone. In the thirty-nine cases in the aneurysm and arterial ligation group, twenty-three or 59 per cent had high tones according to the test. However, three more had definite clinical evidence of high vascular tone, but according to the test were in the low tone group.

It was concluded that the test alone could not serve as the sole basis for selection of cases for sympathectomy. It was found necessary to consider the clinical findings together with the test in order to come to a more accurate conclusion regarding the necessity of sympathectomy.

**Major A. A. Koepsell, De Witt General Hospital: Phlebography in Deep Venous Obstruction.**—Performance of phlebography involves the following elements and considerations: (1) ocular test for sensitivity to diodrast, (2) oral test for sensitivity to diodrast, (3) simultaneous exposures of leg and thigh films after injecting 15 c.c. of the contrast medium, (4) manual pressure or tourniquet about the distal portion of the leg in order to insure that the dye enters the deep venous circulation, (5) tourniquet over the proximal portion of the thigh to be released just before the film of the lower pelvis and upper thigh is exposed, (6) a tourniquet in the axilla or pressure in the supraclavicular region before injecting dye for phlebograms of the upper extremities.

Slides of phlebograms demonstrating the following were shown: (1) severe varicose veins with a normal deep circulation in the leg, thigh, and pelvis; (2) obstruction of the popliteal vein with the formation of extensive collateral circulation; (3) development of extensive collateral circulation after ligation of the deep femoral vein for phlebotrombosis following cellulitis of the foot; (4) deep venous obstruction after excision of a popliteal arteriovenous aneurysm; (5) deep venous obstruction and collateral formation after ligation of the posterior tibial artery and vein following a gunshot wound; (6) patent deep venous system after repair of popliteal vein following excision of popliteal arteriovenous

aneurysm; (7) obstruction of axillary vein following an attempt at repair after excision of an arteriovenous fistula; (8) patent axillary vein following excision of arteriovenous aneurysm with repair of the vein.

**Major Norman E. Freeman, De Witt General Hospital: Treatment of Arteriovenous Aneurysm.**—Before excision of aneurysms and arteriovenous fistulas, careful investigation must be made to be sure that the collateral circulation is adequate to preserve the nutrition of the tissues. At the time of operation, when the lesion has been exposed, additional tests are needed to determine the efficiency of the collateral circulation after the main arterial supply has been cut off. Direct measurements of the pressure within the sac have been made at the time of operation in fourteen patients with arterial aneurysms and arteriovenous fistulas. These measurements have been useful in evaluating the extent of the collateral circulation. The mean initial pressure in arterial cases averaged 97 mm. Hg. With temporary obstruction of the afferent artery the pressure fell to 60 mm. Hg. The lowest level observed which was compatible with adequate circulation was 38 mm. Hg. No disturbances of tissue nutrition were encountered. In arteriovenous fistulas the mean initial pressure was 46 mm. Hg. With temporary occlusion of the afferent artery the pressure fell to 15 mm. Hg, illustrating the catastrophic effects to be expected from ligation of the proximal artery in this condition. Subsequent occlusion of the component veins caused a prompt rise in pressure to 86 mm. Hg in one patient. This level of pressure shows how adequately the collateral circulation is developed in cases of arteriovenous fistulas.

The classical method of quadruple ligation with excision of the fistula has been employed in forty-six patients with arteriovenous fistulas. In eleven, restorative aneurysmorrhaphy was performed by suture of the arterial defect after excision of the fistulas. Success of the repair has been demonstrated by oscillographic readings or by arteriography in each case.

**R. Stanton Sherman, San Francisco: Anatomical Considerations and Treatment of Varicose Veins.**—The anatomy of the deep and superficial veins of the thigh has been studied in 137 anatomic and 703 surgical dissections. The saphenous vein is found to consist of two components, one of which runs part of its course beneath the deep fascia. The two veins unite at, or shortly below, the saphenofemoral junction. The subfascial component is connected with the femoral vein by three main perforating veins—one from the mid-portion of Hunter's canal, one from beneath the sartorius muscle, one from the medial geniculate plexus. Although anatomic variations are common, all arrangements fit into one of four definite plans. It has been found that accessory perforating veins of the thigh may emerge into the superficial fascia without making direct connections with the main saphenous system. The short saphenous vein may be connected with the deep component of the long saphenous and the genicular plexus.

On the basis of the anatomic findings a new operative procedure has been developed. Varices below the knee are thoroughly sclerosed by local injection previous to operation. The usual high saphenous vein ligation is performed along with dissection of the upper tributaries. Retrograde injection is made of a small amount of sclerosing solution. With the aid of a Mayo vein stripper the deep component of the saphenous vein is dissected down to each perforator. The latter are followed to the femoral vein and excised individually.

Convalescence is more comfortable than after simple high ligation with retrograde injection. Patients become ambulatory in twenty-eight hours and leave the hospital in 2.8 days, on the average.

**Howard C. Naffziger, San Francisco: General Considerations in Spinal Cord Injuries.**—There are many ways in which civilian spine injuries compare with the wounds seen in military practice, yet there are points in which they differ. Spinal cord traumatic effects vary from very slight ones to completely disabling ones. Spontaneous repair of true spinal cord injuries does not occur, nor is surgical repair possible. Patients with



complete motor and sensory paralysis caudal to the site of injury for longer than forty-eight hours have little chance of recovery. However, there may be complete paralysis without destruction of the cord. Recovery may occur when the lesion is due to edema. Operative intervention is seldom indicated except to remove foreign bodies or bony fragments. Laminectomy to remove impinging bone fragments or foreign bodies should be performed after compensating for initial shock. There is no known method of repairing the cord by inserting homogenous grafts. Sedulous nursing care to prevent decubitus ulcers is imperative. Ascending genitourinary infections are prevented by providing early adequate urinary drainage. Paraplegic patients succumb to the effects of these latter conditions more than to any others.

**Captain Rudolph W. Zeigler, De Witt General Hospital: Immediate Care of Spinal Cord Injuries.**—A series of forty-one cases is reviewed and the plan of treatment discussed in accordance with the following outline:

1. First-aid Treatment: This includes examination to determine level of injury and extent of dysfunction, which will serve as a basis for comparison with later findings; immediate care of the wound and control of hemorrhage; the administration of analgesic drugs; provisions for safe transportation to prevent further injury; and the recording of accurate notes to accompany the patient.

2. Second Phase of Early Care: This includes measures directed toward prevention of decubitus ulcers, care of the paralyzed bowel and bladder, and institution of replacement therapy when necessary.

3. Selection of Patients for Operation: Decision concerning the advisability of operation is dependent more upon the presence or absence of block to spinal fluid circulation than upon the degree of involvement of the spinal cord as evidenced by neurologic examination. Regardless of the degree of functional impairment of the cord, exploration should be undertaken if there is any degree of block. Aside from indications for operation based on the presence or absence of block, operation should be performed if there is x-ray evidence of pressure upon the cord by displaced bone or a foreign body.

**Major F. H. Benteen, De Witt General Hospital: Surgical Treatment of Decubitus Ulcers in Paraplegic Patients.**—A high proportion of patients with spinal cord injuries incurred in warfare present a sacral decubitus, or ulcers over the femoral trochanters. From the standpoint of general care, these patients require an adequate dietary intake of iron and accessory vitamins to correct the hypoproteinemia, anemia, and avitaminosis that exists. Laboratory aids used have consisted of hemoglobin, hematocrit, and blood protein studies. Adequate nursing care with frequent turning of the patient is of paramount importance in preventing decubiti. Treatment of decubitus ulcers has consisted of mechanical excision of sloughing tissue and chemical débridement with Dakin's solution. Postage-stamp grafts have been utilized occasionally to close a sacral decubitus. Sacral decubiti may be eradicated by excision, followed by widespread mobilization of adjacent skin and subcutaneous tissue, and suture. A sacral decubitus measuring more than 5 by 10 cm. may require flat pedicle grafting accomplished in stages. Smaller decubiti over the greater trochanters may be excised, and skin and subcutaneous tissue mobilized to effect closure. For extensive undermined hip ulcers, it is usually necessary to rotate an adjacent flap to cover the defect and to graft the donor site. It is felt that penicillin is an aid during the period of wound healing.

**Lieutenant Elwyn S. Shonyo, De Witt General Hospital: Ambulation of Paraplegic Patients.**—Early in World War II, Army neurosurgical centers began to develop programs whereby paraplegic patients are made self-reliant and are taught to walk with aid of leg braces and crutches.

The length of the preambulatory period depends primarily upon three factors, namely, the location and severity of fractures of the weight-bearing structures of the spine, the presence of ascending urinary tract infections; and the severity of decubitus ulcers. The presence of decubitus ulcers does not necessarily prevent ambulation.

Ambulation is usually started about three months after the initial injury and the program is carried out in four stages, namely: (1) Bed calisthenics and weight-lifting exercises are given daily, in graduated amounts, to each patient. (2) The patient is placed in a wheelchair where he becomes accustomed to vertical posture. (3) Walking exercises are started with the aid of stiff leg braces using parallel bars for control and support. (4) The patient learns to walk with the aid of crutches.

The extent to which the average patient will use braces and crutches for outside activities after release from hospital care remains to be determined.

**Major Donald C. Malcolm, De Witt General Hospital: Urologic Care of Paraplegic Patients.**—Early measures to prevent urosepsis at the time the patient is most susceptible include uptilting of the torso; turning of the patient every two hours; maintenance of urine specific gravity at less than 1.015; administration of sulfadiazine, 1 Gm. three times a day for the first week, the dose being decreased the next week, and repeated if necessary; administration of 100,000 units of vitamin A daily; and provision of a high protein diet with only moderate milk intake.

Manual expression of urine by suprapubic pressure every three to four hours may be performed during the first few days for patients with cord shock. A suprapubic tube inserted in the vertex of the bladder, and tidal irrigation, assure better progress for the more involved cases. The time for removal of the suprapubic tube varies from a few weeks to over one year. Tidal irrigation aids recovery of reflex voiding. If vesical tone is greater than sphincter and tissue resistance, patients usually void. Probably little benefit is to be derived from presacral neurectomy. Division of the pudendal nerve may relax some perineal muscular resistance. Revision of the vesical orifice serves to remove some tissue resistance. Fumethide, a furfural product, is of some aid in increasing vesical tone.

**Lieutenant Colonel Ambrose H. Storck, De Witt General Hospital: Vocational Rehabilitation of Paraplegic Patients.**—Practically no battle casualties with paraplegia will be able to resume their former civilian occupations, and their physical disabilities greatly limit them in developing new vocations or occupations. The emotional disturbances resulting from their incapacities add to the difficulty of rehabilitating these patients.

The general mental readjustment, the development of new interests, and the learning of new skills or other occupations which are necessary in reacquiring a feeling of economic security and independence as well as a feeling of self-importance should begin as soon as possible following injury. The necessarily prolonged hospitalization of paraplegic patients in Army General Hospitals requires that the rehabilitation process be at least started in such hospitals.

To assist patients in finding themselves and in selecting new vocations and occupations in keeping with interest, skill, and mental capacity, an interviewing and testing program was established. The patient's civilian occupation is considered; his Army general classification test given at the time of his entry on military duty serves as an index of pretraumatic intelligence; a Kuder preference record is made to gain insight into interests; an Otis self-administered classification test furnishes additional data concerning intelligence; a MacQuarrie mechanical aptitude test is employed to reveal aptitude and dexterity; a Rorschach psychodiagnostic test (group) is used to indicate personality features; and practical "test" classes are given in art, plastics, jewelry making, wood carving, and ceramics.

On the basis of interviews and tests the patients are given instruction and afforded other facilities which enable them to pursue their interests, skills, or other vocational desires. In addition to instruction in arts and crafts, educational programs include general academic, typing, and small business accounting. As a part of the general education and orientation provided, authoritative talks by well-informed speakers have been given or

requested on the following subjects: Postwar California, Commercial Art, Plastics, Office Engineering, Taxidermy, Lapidary Work, Saddlemaking, Bookkeeping for Small Business, Business Trends in California, Retail Outlets for Homemade Articles, Experience Stories by Handicapped Persons, and General Economic and Social Problems.

In addition to the medical officers of various sections, cooperating members or departments of the hospital staff include the counseling officer, the orientation and education department, the occupational therapy staff, and the psychologist.

Outside agencies which have assisted in the program at De Witt General Hospital include Placer College and High School, which has supplied teachers; California Veteran's Committee, which has taken an interest in the matter of making contacts and sponsoring appropriate legislation; the Sacramento Junior Chamber of Commerce, which has furnished speakers; the California State Personnel Board, the California Board of Equalization, and the California Department of Public Works which have been concerned with the matter of jobs.

Funds for the purchase of special instruments and equipment necessary in training for various crafts have been made available through interested individual donors.

In conjunction with physical rehabilitation and purely recreational activities, vocational rehabilitation has resulted in transformation of paraplegic patients from a state of listlessness, discouragement, and dejection, to one of animation, interest, hopefulness, and as much happiness as could well be expected.

**Alton Ochsner, New Orleans: Surgical Treatment of Empyema.**—Treatment of empyema can be divided into prophylactic and active therapy. Prophylactic treatment concerns principally the prevention of contamination during thoracic operations, along with preoperative and postoperative chemotherapy. Active treatment consists of chemotherapy, relieving intrathoracic pressure, evacuating pleural exudate, preventing chronicity, and reestablishing function in the lung. In prophylactic as well as active treatment penicillin is used both systemically and locally, whereas sulfonamides should be used only systemically. Because of loss of nitrogenous substances in pleural exudate, diet should be rich in proteins. Important also is the prevention of anoxia. Pleural effusions on the right side are likely to kink the inferior vena cava and cause cardiovascular manifestations.

Evacuation of intrapleural exudate should be accomplished as early as possible. In syneumonic empyema, repeated aspiration combined with chemotherapy is the proper treatment but if symptoms do not subside promptly more radical therapy is necessary. Closed drainage may be used early. Its advantages are that it re-establishes normal relations in the thorax, favors lung re-expansion, and facilitates irrigation of the cavity. Disadvantages of closed drainage are the constant supervision required, the likely inadequacy and chronicity thereby favored, and the danger of intramural infection. In most cases of metapneumonic empyema, open drainage is desirable. Advantages of open drainage are adequate evacuation of intrapleural exudate, with resulting lessening of danger of chronicity, and little supervision required. Disadvantages of open drainage are that open pneumothorax results, re-expansion of the lung is not favored, and deformity of the chest may follow. In performing open drainage a good portion of two ribs and the intervening intercostal bundles should be removed.

**Captain F. W. Rhinelander, Hammond General Hospital: Surgical Reconstruction of Arthritics.**—Rheumatoid arthritis is obviously a medical disease, and must be under the primary care of an internist. The orthopedist can do considerable during the course of the disease to prevent deformities, and sometimes to lessen them, without recourse to surgery. But despite the best conservative treatment, when the disease becomes advanced, certain crippling deformities may develop. Those patients who have advanced forms of the disease do not expect to be cured. But they are very grateful if something can be done which makes their lot easier—reduces the pain which they have when attempting to carry out their daily activities.

Certain operative procedures were discussed. In the foot, resection of the metatarsophalangeal joints yields best results when all four lateral joints are fully excised, plus resection of the base of the proximal phalanx of the great toe. Other occasionally valuable operations are triple arthrodesis of the foot, arthrodesis of the ankle or knee, synovectomy of the knee, arthrodesis of the shoulder. Capsulotomy of the small joints of the hands cannot give greatly improved motion, but it can make a patient better able to wring out her washing. Rather than arthrodesis of the wrist, it is generally better to manipulate the painful and stiff wrist into good position, and hold it in plaster until it fuses. Arthroplasty or excision of the elbow gives excellent results, the latter more frequently because it eradicates more diseased tissue. Simple excision of the radial head may lead to increased rotation and decreased pain.

Some cases in which Smith-Petersen had performed vitallium cup arthroplasty of the hip, and osteotomy of the articular facets and laminae of the spine, were presented with lantern slides. These procedures are valuable even if they do no more than make a bedridden patient able to sit up or get about on crutches.

The chief thing to remember in operating on patients with arthritis is that if only a little can be done to improve them, it is extremely worth while.

**Sterling Bunnell, San Francisco: Reconstructive Surgery of the Hand.**—There are many things, starting from the time of injury, that should be done to avoid stiffening. Anatomically the hand is to be considered not as a unit at the wrist, but as a unit up to the elbow. The muscles that move the hand have their origins largely from the elbow. Dynamically the hand should be considered as starting from the cerebral cortex. Thought must be given to early closure of wounds to prevent the cicatricial effects of chronic infection. In the event of extensive tissue damage and likelihood of infection, primary débridement with secondary closure of the wound is to be performed. Fractures should be reduced early. The hand and finger must be supported in the best functional position and mobility of the hand and forearm is to be instituted at the earliest possible time. Elastic splinting and traction is a great advance over the fixed type of support. All of the hand should be put in a functional position and kept moving.

Meticulous care is to be used in approximating the nerve fibers of the hand. Tendons must be provided with smooth gliding surfaces to prevent fixation by adhesions. The principle of repair after severance of a tendon is that of mere approximation of the ends by a few fine sutures, while the tension is removed by means of a steel wire suture taken through the proximal portion. The free ends are brought out distally and fastened over a button. A second wire loops through the proximal portion so that the retention button may be removed in three weeks, and the wires withdrawn from the proximal muscle and tendon.

Considerable effort should be made to reconstruct the thumb, providing a more useful hand. A finger may even be substituted for a missing thumb by metacarpal union and tendinous attachment.

**Lieutenant Colonel Edward K. Prigge, De Witt General Hospital: Experiences in the Management of Chronic Osteomyelitis Following Compound Fractures.**—A method employed in the treatment of osteomyelitis following compound fractures is presented. In general it consists of radical excision of all avascular scar, sinus tracts with contained chronically infected granulation tissue, sequestrums, and eburnated or otherwise abnormal bone. In areas where the involved bone is encased by muscle (back, arm, forearm, thigh, and forefoot) the space remaining after excision is filled with viable muscle, either by displacement of adjacent muscle or by formation of a pedicle of available muscle. No dead space is allowed to remain. In areas such as the lower forearm, the tibia, and the tarsal bones, the defect is filled with cancellous iliac bone graft after three weeks of local and systemic penicillin therapy.

In thirty-five consecutive cases in which muscle was used to fill the defect, the results are very gratifying. A thin serous exudate continued to drain in only one case;

this will require subsequent excision. One patient had drainage for two months. The other thirty-three were completely healed between two and five weeks. The average period of drainage prior to surgical excision was 5.6 months; the average period of drainage following operation was 3.9 weeks. There were seventeen ratable cases where cancellous iliac bone graft was used to fill the defect. In ten patients, in whom the defect was less than 3 to 5 cm. in diameter, eight are completely healed and one nearly so. In the seven with larger defects, none have been successfully healed to date, although the iliac graft appears to be viable to inspection and by x-ray.

In all, fifty-two consecutive patients with chronic osteomyelitis following compound fractures have been treated by the two methods described; there was an early healing of the disease in 84.6 per cent of the cases. It is felt that with improvements in technique and better selection of cases, these results can be improved materially.

**Captain E. V. Davis, De Witt General Hospital: Treatment of Severe Elbow Injuries.**—Severe disruptive injuries of the elbow joint result in a painful stiff joint if not treated early by accurate reduction in order that early mobilization can be instituted. If normal configuration of the joint cannot be restored, excision of the joint prior to the development of atrophy, muscle weakness, and causalgia is indicated.

In late cases, when ankylosis has developed, excision rather than arthroplasty is recommended because even though the joint is not as stable after excision, mobility and muscle power are superior.

The operation is performed through a posteromedian incision. Sufficient bone is removed from the distal end of the humerus and the proximal ends of the radius and ulna to allow a minimum of  $1\frac{1}{2}$  inches of dead space between them. A fascial graft from the thigh is used to cover the lower end of the humerus.

In summary, I have observed twenty excisions of the elbow. There were no infections. The range of motion varied from a complete range to a minimum of 55 degrees. One patient returned to work as a stevedore. All were free of pain and were satisfied with the end result.

**Major Manuel Sall, De Witt General Hospital: Diagnosis of Herniation of Nucleus Pulposus.**—Fifty-three cases proved by operation or by myelogram alone were reviewed. Ninety-three per cent of these cases involved the fourth and fifth lumbar and fifth lumbar to first sacral levels. A history of antecedent back trauma with the development of back pain and referred root pain was the usual history obtained. In one patient pain was limited to the low back. The most commonly encountered distribution of pain involves the low back, with referral to the mid-gluteal region and down the posterior thigh, leg, and lateral ankle and foot due to involvement of the first sacral root. Changes in the alignment of the vertebrae with scoliosis and loss of the lumbar curve are found in the most acute cases. Atrophy of one leg was frequently observed, the degree of atrophy appearing to bear a relation to the duration of the painful episodes. In subacute cases initial flexion of the trunk was performed without significant difficulty, increasing back pain being encountered with more extreme degree of flexion. Extension of the spine is occasionally limited to a striking degree. Areas of focal spinal tenderness may serve as an excellent means of localizing the level of the disc protrusion. In twenty-eight cases in which this sign was sought for, twenty-two patients revealed focal tenderness at a level corresponding to that found at operation or by myelogram. Placing the sciatic nerve on stretch invariably aggravates the pain. Weakness of dorsiflexion of the foot or extension of the great toe should be sought for. An unusual finding in a few cases has been a noticeable weakness on initiation of dorsiflexion of the foot. Testing for power of dorsiflexion following the initial phase of the movement in these cases failed to reveal significant weakness. In one patient on whom operation revealed a large protrusion at the fifth lumbar to first sacral level the only clinical findings were focal tenderness between the two, and weakness of the initial phase of dorsiflexion. Hyperesthesia to pin stroking is a valuable aid in diagnosis and localization. Differences in degree rather than absence of sensation is the usual finding.

Too often, painful pricking with a pin and the patient's acknowledgment of pain is accepted as evidence of normal sensation. The achilles reflexes were found to be absent  $2\frac{1}{2}$  times more frequently in the fifth lumbar to first sacral than in the fourth to fifth lumbar discs. Of great value is a difference in reflex response which frequently can be obtained only by the use of minimal stimulation of the achilles tendon. Spinal fluid protein above 45 mg. per cent was found in about 20 per cent of the cases. It is believed that a diagnosis and satisfactory localization of a herniated disc can be made on the basis of clinical examination alone in the vast majority of cases.

**Lieutenant Commander F. Keith Bradford, U. S. Naval Hospital, Oakland: Surgical Treatment and Prognosis of Protruded Intervertebral Disc.**—Any discussion of surgery upon the ruptured intervertebral disc must presuppose rigid selection of patients for operation.

Spinal anesthesia is highly satisfactory although its use might be criticized in the occasional patient with sphincter paralysis. The usual unilateral subperiosteal laminectomy has been routine. At the lumbosacral intervertebral disc little if any bone need be removed for adequate exposure, but at higher levels partial hemilaminectomy is necessary. Adequate exposure is essential and is possible without removing a spinous process or lamina. It is never wise to approach the dural sac directly with an attempt to retract it medially in the face of inadequate lateral exposure; extensive cauda equina damage may result, but has never followed mobilization started lateral to the involved root. Transdural attack upon ruptured discs can never be condoned. It would be better, if necessary, to sacrifice a single root in order to retract the dural sac medially.

Recognition of true surgical pathology is probably the most important factor in disc surgery. Either the presence of nucleus pulposus posterior to the annulus fibrosus or the presence of a laceration of the annulus fibrosus (neither created by the operator) is irrefutable evidence of a ruptured disc. Herniations which do not appear prominent in the prone position have been shown to project in a prominent manner when the patient has been operated upon in a sitting position. However, it is felt that adequate exposure with the patient in the prone position determines whether an additional interspace must be explored to find the cause of the patient's symptoms.

No surgeon, however able technically, can obtain a good percentage of favorable results in patients selected uncritically for operation. Conversely, inadequate or needlessly traumatic exploration in well-selected patients will produce unsatisfactory results. Since the initial operation offers the best opportunity for cure of the patient, it must be undertaken carefully and thoroughly only after complete study of the patient.

**Lieutenant Colonel William R. Lipscomb, De Witt General Hospital: Correction of Cranial Defects.**—Skull defects can be corrected in several ways. An old method was by use of bone grafts. Unfortunately, many of the free grafts, taken from tibia, ileum, sternum, or rib, were absorbed or infected and had to be removed. Hinged osteoperiosteal and hinged scalp osteoperiosteal grafts have been more successful. Various metals such as silver, gold, aluminum, platinum, columbium, and vitallium have been used. Methyl methacrylate, a resin, has also been used in correcting cranial defects. Tantalum has been the material most widely used in World War II. It possesses very desirable physical and chemical properties. It is strong, but malleable, and can be beaten and bent into any shape to conform to normal skull contour. Tantalum reacts chemically with no body tissues or fluids. Preformed tantalum plates can be layed over the skull defect and fixed in position by tantalum pegs driven into the surrounding skull as a glazier fixes a pane of glass with metal pegs.

In the last seventeen months, over eighty tantalum cranioplasties have been done at De Witt General Hospital. The results have been gratifying. Frequently the patients remark on loss of former vertigo and pulsations in the head associated with exertion. All patients appreciate the cosmetic improvement. The most noticeable improvement is usually in personality. An appearance of happiness replaces the depressed, concerned expression. This improvement is not limited to those patients with frontal lobe damage.

**Lieutenant Bertram Selverstone, De Witt General Hospital: Peripheral Nerve Repair.**—It has been estimated that 10.5 per cent of casualties in World War II have lesions of the peripheral nerves. The distribution of these lesions is quite similar to that of World War I. Pathologically, partial and complete lesions are distinct entities, but it is often impossible to decide before operation whether or not a lesion is complete. Clinical examination includes muscle test and observations concerning sensation and sweating. Tinel's sign may be of value in following the progress of regeneration after suture, but is unreliable preoperatively. (Faradic, galvanic, and sinusoidal electrical examination together with electromyography and skin resistance tests are valuable adjuncts. Stimulation is particularly important in evaluating a lesion at the operating table.

The policy at De Witt General Hospital has been: (1) early exploration if there is not rapid and progressive improvement; (2) conservative management of the exposed lesion; (3) re-exploration indicated and desirable if improvement does not occur in six to twelve weeks following neurolysis; neuroorrhaphy shows no evidence of return in period consistent with site of lesion; (4) avoidance of nerve grafts since they are rarely necessary; reported results have not been favorable.

Technical problems are concerned chiefly with gaining length to replace lost nerve tissue, orientation of nerve ends, and protection of the suture site. Suture with tantalum wire and wrapping with tantalum foil has usually been employed, although in several cases the plasma clot technique of Tarlov has been used. Results have been favorable in patients operated upon six or more months ago.

**Captain Jerome L. Sweeny, De Witt General Hospital: Management of Combined Bone and Nerve Lesions.**—In treating an extremity in which a bone and a nerve lesion coexist, treatment should be directed first to repair of the nerve. Grafts may be done at any time without materially affecting the use of the extremity, whereas the sooner the nerve is repaired the better are the chances of regeneration, with minimal atrophy of affected muscles.

On occasions, combined orthopedic and neurosurgical procedures may be done at the same operation as, for example, a graft to the humerus and a bulb suture of the radial nerve. This is done only when end-to-end nerve suture is not possible. By such a procedure, the patient is saved an additional operation and hospitalization is shortened. The grafting of a fractured humerus as a primary procedure often delays nerve repair for a period of months. The immobilization necessary after bone grafting frequently results in a stiff joint, and physiotherapy over a considerable period of time may be required to mobilize the joint sufficiently to make end-to-end nerve anastomosis possible. Nonunion of the bone may be taken advantage of either to buckle the fracture site so as to gain length for neuroorrhaphy, or bone ends may be jammed together to reduce the distance between nerve ends, thereby making end-to-end suture possible.

**Second Lieutenant Joseph M. Wepman, De Witt General Hospital: Re-education of Aphasia Patients.**—The entire history of therapy for patients having language disorders as a result of brain injuries is concentrated in the last two or more decades. With new emphasis on training has come a new philosophy toward the prognosis for language return—that every patient can be benefited and that the limitations upon improvement are by virtue of the extent of intellectual impairment.

The program designed and functioning at this Army installation includes at least six hours of daily instruction for each patient. This therapeutic process includes speech therapy, both individual and group; reading; writing; occupational therapy; physiotherapy and swimming. Each patient has an individual program to follow, adapted to his needs.

At the initiation of therapy each patient is assigned to a particular therapist who is responsible for his entire corrective course, establishing a rapport and a working identification which has resulted in excellent achievements.

A typical program for a patient with head injury begins with a complete physical and neurologic examination. He is then seen by a psychologist who measures his in-

intellectual potential and degree of impairment by means of a test designed here by the chief of the neurological section and myself. The patient is then given a Halstead aphasia test to delimit his language disability. Following this he is assigned to a therapist and is seen twice daily for speech therapy, once individually and once in group session. He is entered in a reading class, a writing class and a swimming class. He is assigned to occupational therapy with a prescription that is designed to increase his co-ordinative abilities and finally is sent to physiotherapy for at least one hour a day. With this approach there is little time for the patient to develop self-concern or anxiety over his condition.

The results of this highly developed but very flexible method of handling the aphasic patient have been excellent. Every patient that has been seen has shown improvement and continues to develop in the direction of normal speech.

**Major Walter E. Scribner, De Witt General Hospital: Roentgen Findings in Peptic Ulcer.**—In approximately 1,500 stomach examinations during a period of three years, I have seen only about ten gastric ulcers. The usual x-ray finding in gastric ulcer is a barium-filled protrusion from the lesser curvature of the stomach, about which there is a zone devoid of barium, the barium-free zone representing edema of the gastric mucosa. As healing takes place the edema decreases, and scarring in the mucosal folds causes a convergence of the folds toward the healing ulcer. Convergence of the rugal folds resulting from scar contracture is, therefore, an index of chronicity of the ulcer.

Duodenal ulcer is, in my experience, the greatest cause of peptic disability in the Army. The classical roentgen findings of duodenal ulcer, such as visualization of a crater, adjacent inflammatory, spastic, and cicatricial changes in the bulb, and the secondary changes in the stomach proper, were discussed with recommendations for special spot compression films in those patients with deformities which obscure the crater. Localized tenderness, hyperperistalsis, increase in thickness of gastric rugae, and hypertonus, were of no independent value in the diagnosis of duodenal ulcer.

A warning note was sounded, to be kept in mind in those patients who had ulceration or deformity just proximal to the pyloric ring. Because some may show pyloric canal deformity as the most prominent feature, early carcinoma in the region may be erroneously diagnosed as pyloric ulceration.

**Major Jerry J. Kane, De Witt General Hospital: Diagnosis and Medical Regimen in Duodenal Ulcer.**—Four hundred eighty-eight patients were hospitalized in the gastrointestinal section at De Witt General Hospital, from Aug. 1, 1944, to August 1, 1945, because of dyspepsia. A diagnosis of peptic ulcer of the duodenum was made and verified by roentgen studies in 187 patients, or 38.3 per cent. The pre-eminent symptom in this group was epigastric pain, described as "burning" or "gnawing" in character, with the majority of the group exhibiting the characteristic cycle of pain—food—relief. Only three cases demonstrated an absence of this rhythm. One hundred eighty of these patients had had overseas service. All complained of nausea and vomiting besides epigastric pain. The symptoms of nausea and vomiting usually disappeared in five days, and from then on were invariably absent. Two per cent of this group gave a history of pain over McBurney's area, and had had appendectomies without relief. All of the appendectomies had been performed in civilian life. One hundred seventy-eight patients had had episodes prior to military service, over an average period of approximately six years. Patients were practically unanimous in describing their attacks as being more frequent and more severe since being in the service. Thirty-two patients had night pain occurring between 2:30 and 3 A.M.

Each patient in this group was kept in the hospital approximately thirty days, during which time he was placed on a modified Sippy regime. The majority were returned to civilian life.

**Alton Ochsner, New Orleans: Physiologic Treatment of Peptic Ulcer.**—Etiology of peptic ulcer may be divided into predisposing and precipitating factors. Principal predisposing factors are tissue susceptibility and constitutional predisposition, neither being



generally amenable to therapy. Tissue susceptibility is present in all individuals and is found in lesser curvature of stomach, pylorus, duodenal cap, and that portion of the intestinal tract subjected to acid gastric chyme. Constitutional predisposition is probably the most important cause of peptic ulceration, and the patient who has an ulcer tendency is likely to have an ulcer the rest of his life unless he avoids precipitating factors. The precipitating factors are important because they are amenable to therapy. They consist of gastric hypersecretion and hyperacidity, focal infection, and trauma.

Treatment is based upon concept that hyperacidity is the principal responsible factor amenable to therapy. Control of hyperacidity by prophylactic measures is extremely important and consists of (1) total abstinence from smoking, (2) total abstinence from alcohol, (3) avoidance of condiments, and (4) moderate ingestion of meats. Active therapy of hyperacidity consists of frequent small feedings. During active ulceration antacids are indicated, and of greatest value is aluminum hydroxide. Foci of infection should be removed. Gastric trauma should be prevented by avoiding irritating rough foods, and antispasmodics should be administered.

Requisite for successful therapy of a chronic peptic ulcer is conviction of the patient that the ulcer diathesis persists during his entire life, and recognition by him of the importance of avoiding all controllable precipitating factors for the rest of his life.

Surgical therapy of peptic ulcer consists principally of treatment of complications, that is, perforation, pyloric obstruction, massive hemorrhage, and suspected malignant change. About 5 per cent of duodenal ulcers will not respond to conservative therapy, and in this resistant group gastrectomy is justified. Treatment of perforation consists of suture of the ulcer or of plugging with omentum. Treatment of pyloric obstruction depends upon the presence or absence of anacidity. In older persons with anacidity, gastrojejunostomy is indicated because the possibility of return of normal acidity following relief of gastric retention is less than in younger persons. In individuals with normal acidity or hyperacidity, subtotal gastrectomy should be done. Massive hemorrhage, before the age of 50 years, is best treated during the acute phase by conservative measures consisting of repeated transfusions, the administration of cevitamic acid, and frequent feedings. After the age of 50 years gastrectomy is frequently indicated during the acute hemorrhage because of danger of hemorrhage continuing as a result of sclerotic, non-contractile vessels. Mortality following conservative therapy in older persons is over 30 per cent, whereas following gastrectomy it is less than 10 per cent. In the younger person who has had a massive hemorrhage, gastrectomy is usually indicated after the hemorrhage has been controlled and the patient rehabilitated.

Gastric ulcers should be considered primarily as surgical lesions because of the great tendency for them to become malignant. All greater curvature ulcers must be considered malignant from the beginning. The incidence of malignancy of the stomach in patients who have family history of ulcer is much greater than in other individuals.

**Major Richard B. Capps, De Witt General Hospital: Surgical Significance of Hepatitis.**—Infectious hepatitis is of importance to surgeons because of the danger of operating in unsuspected cases. This may have fatal results. Acute abdominal symptoms are not uncommon. Avoidance of inhalation anesthetics is important. Morphine and other sedatives are to be avoided. Finally, chronic cholecystitis is frequently confused with chronic infectious hepatitis. The Graham-Cole test may show an absent shadow in the latter condition.

Infectious hepatitis has become, during the last four years, an important problem. Not only has there been a high incidence among the armies of the world, but there has been a marked increase among civilians in various countries. It is now known that this disease is due to a filterable virus transmitted chiefly by the enteric route and also through plasma and whole blood. It is important to recognize that there is a nonicteric prodromal stage, lasting about seven to ten days in most acute cases. Furthermore, there are many patients with mild acute cases, who never develop either clinical or chemical icterus. We have demonstrated, furthermore, that convalescent patients cannot be con-

sidered as cured until subjected to a seven-day exercise tolerance test. Patients apparently well at bed rest or on minimal exercise frequently develop a large, tender liver and a recurrence of symptoms following exercise. Essential treatment consists of bed rest and a high protein diet.

**Captain Melvin B. Kirstein, De Witt General Hospital: Blood Diastase and Acute Abdominal Pain.**—It is now known that in addition to the fulminating type of acute pancreatic necrosis, a milder, more common type of inflammation frequently occurs. This has been termed "acute transient pancreatitis" by Elman.

Twenty such cases have been observed and elevated blood diastase values ranging from 250 to 3,200 were found. This test was performed by the method of Somogyi, in which the normal blood diastase ranges between 80 to 180 units.

All patients with acute transient pancreatitis showed an elevated blood diastase, provided the determination was made sufficiently early in the disease, and all patients recovered. In acute pancreatic necrosis, the blood diastase value may later become normal, even though the patient is dying. This is explained on the basis of the pancreatic necrosis progressing to such a point that the pancreas is not capable of influencing blood diastase. In acute transient pancreatitis, the inflammation may be so transient that a rapid return to a normal blood diastase value precedes the disappearance of abdominal pain. It is, therefore, necessary to perform the test early in the disease. Blood diastase values are also elevated in acute diseases of the salivary glands and in severe renal disease.

It is safe to conclude that any patient who has severe abdominal pain, a blood diastase value (Somogyi method) over 250, with no evidence of acute salivary gland disease or renal insufficiency has acute pancreatitis.

It has been our custom not to operate on patients with acute pancreatitis of any type. Patients are treated by parenteral fluids, morphine for pain, and no food.

**Charles Edward Smith, San Francisco: Current Problems in Pulmonary Coccidioidomycosis.**—Knowledge of coccidioidomycosis has been broadened through the activities of the Commission on Epidemiological Survey of the Army Epidemiological Board, Preventive Medicine Service, Office of the Surgeon General and of the Office of the Air Surgeon. Studies of distribution reveal no infections outside the Western Hemisphere and delimit its occurrence in southern and western Texas, Arizona, southern Utah, Nevada, and California. The army experience has indicated coccidioidomycosis can be classified as follows: (1) Primary or initial (a) inapparent or asymptomatic (50 to 67 per cent), (b) acute respiratory or pneumonic (33 to 50 per cent), (c) additional manifestations of either of these; erythema nodosum and/or multiforme (3 to 5 per cent); pleurisy with effusion; pulmonary cavitation. (2) Progressive or disseminated (0.2 per cent whites; 2 per cent colored). Differentiation of coccidioidal pulmonary nummular lesions and cavities from tuberculosis is difficult. Steps in diagnosis are: (1) Coccidioidin test. If either tuberculin or coccidioidin fails to react while the other reacts, diagnosis is well underway. However, frequently both react. (2) Serologic tests. Precipitins, seen usually in initial infections, are lacking in old infections. With the well-focalized nummular coccidioidal lesions and many cavities, complement fixation is also lacking. Positive findings are diagnostic; negative findings do not eliminate coccidioidomycosis. (3) X-ray examinations. Findings may be confused with various forms of tuberculosis. If the tuberculin test is positive, accurate evaluation is necessary. (4) Recovery of the fungus. Demonstration in tissues of double-contoured spherules with endospores and no budding, is diagnostic. Cover-slip examination is unreliable and staining of smears is useless. Culturing sputum or gastric contents usually fails in nummular lesions but succeeds with cavities. Although hazardous, demonstration of the diphasic fungus, *Coccidioides immitis*, is conclusive.

**Major Robert A. Chait, De Witt General Hospital: Penicillin Therapy in Chronic Sinusitis.**—This study was undertaken in order to determine the effectiveness of penicillin in the treatment of chronic infection of the maxillary sinuses by local application of the drug.

A diagnosis of chronic, purulent, maxillary sinusitis was made in 114 patients on the basis of history, clinical findings, transillumination, x-ray, and the presence of pus on puncturing and washing the sinuses. The maxillary sinuses were irrigated with 130 c.c. of sterile saline solution through a 15 gauge straight needle introduced through the inferior meatus, and 15 c.c. of penicillin solution containing 250 units per cubic centimeter (pH = 6.5) were instilled into the sinus. These 114 patients had their antra treated in this manner 526 times, treatments being given three times weekly.

Patients were considered to be "cured" when the symptoms and signs of infection had disappeared, when transillumination and x-ray showed the sinuses to be clear, and when antral washings were clear and culture showed no growth of bacteria.

In 95 per cent of the patients returns were clear after two to four irrigations. A few required five to nine washings. All but one were completely cleared of the infection, that one having a mixed bacterial flora which was penicillin insensitive. All washings were cultured and penicillin sensitivity tests done. The organisms found at culture included *Staphylococcus albus*, *Streptococcus viridans*, hemolytic streptococcus, *Staphylococcus aureus*, *Aerobacter aerogenes*, *Escherichia coli*, *Hemophilus influenzae*. Nearly all washings were reported as sterile after the second, third, or fourth washing.

It is concluded that penicillin employed locally according to the technique outlined has proved to be effective in the treatment of chronic sinusitis.

**Harold H. Lindner, San Francisco: Anatomical Considerations in Inguinal Hernia.**—The presentation of these data was emphasized by reference to three anatomic specimens which illustrated the points made. Important anatomic points include the attachment of the inguinal ligament to the pubic tubercle and to the iliopectineal line by the lacunar ligament, expected variations that occur in the formation of the conjoined tendon, and the role of the transversalis fascia. The transversus abdominal muscle does not fill in the posterior floor of the inguinal canal and the transversalis fascia is modified in this area to protect the floor of the canal. In order to secure an adequate anatomic repair, the transversalis fascia should be utilized with its attachment to either Cooper's and the lacunar ligament or to the shelving edge of Poupart's ligament, depending upon the laxity of the structures involved. The mode of production of hernial sacs was discussed and the anatomic points were presented, clarifying the reasons why direct and indirect sacs are occasionally misinterpreted on clinical examination.

**Major Frederick H. Benteen, De Witt General Hospital: Repair of Primary and Recurrent Hernia.**—The incidence of inguinal hernia is considered to be about 2.4 per cent in the male population of military age. Published statistics of over 100,000 repairs of primary and recurrent inguinal hernia show recurrence rates of 8 per cent in indirect hernias, 15 per cent in direct hernias, and 20 per cent in recurrent hernias. Adequate hemostasis, the use of fine suture material, clean anatomic dissection, and avoidance of tension are necessary to assure wound healing. Suture of the transversalis fascia or conjoined tendon to Cooper's ligament following extirpation of the sac is ordinarily the basis for the cure of inguinal hernia. However, it is felt that no single method of hernioplasty is invariably adequate to reconstruct satisfactorily the abdominal wall around the cord. Fascial strips from the external aponeurosis, fascial strips from the thigh, or fascial patches from the thigh may on occasions be used as grafts. A relaxing incision in the anterior rectus sheath is sometimes indicated. Employment of a flap of anterior rectus sheath or a flap of fascia lata left attached to the donor site is not desirable. Bone periosteal grafts have been used in reconstruction, and the cord has been placed in various positions, including transplantation to a femoral location, but it is felt that such procedures are not necessary.

**Major Gordon C. Langsdorf, De Witt General Hospital: Administration of Fluids, Including Plasma and Blood, in Prolonged Surgery.**—A surgical patient, who is draped and under a battery of operating lights in a room not air-conditioned, suffers enormous

fluid and salt loss during a five- to ten-hour operation, particularly during the hot summer months. Salt and dextrose solutions are primarily useful for the correction of resultant dehydration but not as blood substitutes. Sodium chloride must be held to a minimum and the remaining fluids given as 5 and 10 per cent dextrose in distilled water to prevent excessive fluid retention and pulmonary edema. Plasma is used to tide a patient over a period of unexpected severe blood loss while whole blood is being obtained for transfusion. True maintenance of a patient during a "bloody" operation requires constant intravenous replacement of whole blood. Experience has reemphasized the advisability of carefully placing one and in some instances two large gauge needles or cannulae into appropriate veins in the forearm or ankle before operations such as lumpectomy, craniotomy, and aneurysmorrhaphy are commenced.

**Lieutenant Colonel Irving Madoff, De Witt General Hospital: Laboratory Adjuncts in Transfusion.**—Types of transfusions for specific purposes are classified as (1) autotransfusion, (2) immunotransfusion (specific and nonspecific), (3) exsanguinotransfusion, and (4) reciprocal transfusion.

The various techniques of blood typing are discussed, with emphasis on the points that all cell suspensions used should be as fresh as possible, kept refrigerated, and prepared with sterile equipment. These precautions prevent loss of sensitivity and protect against contamination.

Dried rabbit typing sera are the standard routine typing materials used. The necessary precautions and pitfalls involved are pointed out. Compatibility tests require expert judgment in order to prevent reactions. The method used in this laboratory is a modification of the Levine method, in which the tests are done at refrigerator, room, and incubator temperature and then centrifuged. This enhances the sensitivity of the reaction and detects "cold" agglutinins. Among the complications of compatibility tests are autoagglutination, panagglutination, rouleaux formation, drug effects, and multiple transfusions. The main types of transfusion reactions are thermal, hemolytic, and hemorrhagic.

A blood bank is operated in which, based upon local experience, certain percentages and types of blood are both stored and ordered, in advance of use. Rh tests are routine and only homologous bloods with the same Rh factor are used. This system enables the bank to dispose of 90 per cent of the blood on hand in less than three to four days. The transfusion service is informed at all times of any special precautions in the handling of individual bloods. In multiple transfusions recross-matching is recommended after each individual transfusion. Transfusion equipment should be prepared and handled only by conscientious, experienced personnel.

A recent development is the use of plasma skin sensitivity tests in the detection of allergic responses. Whole blood should not be transfused immediately after pooled plasma administration, as heterologous agglutinins may have been introduced, thus possibly causing a reaction. If whole blood transfusion is necessary immediately following plasma administration, only "O" blood should follow the use of plasma.

# Book Reviews

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**Orthopedic Surgery.** By Walter Mercer, M.B., Ch.B., S.R.C.S., S.R.S. Pp. 447, with 415 illustrations. Baltimore, 1943, Williams & Wilkins Company. \$12.

The new edition of Mercer's *Orthopedic Surgery* represents a rather extensive revision of the previous editions. There is a general improvement in illustration, and the material has been carefully revised with the incorporation of many new and original ideas, plus recent advances in orthopedic surgery as gleaned from the literature. There has been some deletion of material which the author no longer considers relevant.

The sections which appear to have been the most completely revised are those on the affections of the back, knee, shoulder, and foot and infections of the hand. The description of some of Brittain's operations on joints and his methods of arthrodeses, plus Iselin's work on infections of the hand are incorporated into the appropriate chapters.

Some of the subjects which are covered most thoroughly and efficiently are the developmental affections of bone and joint, circulatory lesions of the extremity, manipulative surgery, arthrodesis, and arthroplasty. The discussions on the regions of the body which are especially well covered are those of the spine, shoulder, and knee. The particular section on complications from trauma is exceptionally well written. This book is a compilation of the material used in lectures in clinics on orthopedic surgery as conducted by the author under the direction of Professor Fraser, and the bibliography is not all inclusive nor comprehensive but does refer to authoritative and recent articles, in both the British and American journals.

It is an excellent book. This third edition is more comprehensive than the former two editions, and far more complete than any of the various books on orthopedic surgery written in the United States at the present time. One may question the emphasis placed on tuberculosis of bones and joints and criticize the relatively brief discussion of herniated nucleus pulposus as a cause of back pain. This book deserves its place as a standard text in orthopedic surgery and should be in every orthopedist's and pediatrician's library.

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**Fractures and Orthopedic Surgery for Nurses and Masseuses.** By Arthur Naylor, Ch.M., M.B., M.Sc., F.R.C.S. (Eng.), F.R.C.S. (Edin.). Pp. 280, Baltimore, 1945, Williams & Wilkins Company.

This is an excellent book which serves as an introduction of orthopedic surgery and fractures to nurses and physiotherapists. No nursing techniques are described and no attempt is made to emphasize nursing care of orthopedic and fracture patients. The emphasis has been placed on the general principles of surgery and their application in orthopedic surgery. In short, this book does not attempt to explain how the nurse is to care for the patient but rather what the basic principles of the various diseases are that she must understand to care for the patient properly.

The book is well written, interesting, and concise. The illustrations are good and the diagrams are of exceptional clarity and interest. The book will serve the medical student as a supplement to any of the more complete and comprehensive texts in orthopedic surgery. The reviewer feels that it would be of more value in this respect than any of the synopses or short texts written on the subject in this country. Since it is written from a British viewpoint some of the procedures described are unfamiliar and a few of the apparatuses are generally considered obsolete in this country.

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